543,177

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
5 August 2004 (05.08.2004)

PCT

(10) International Publication Number
WO 2004/065370 A1

(51) International Patent Classification[7]: C07D 235/18

(21) International Application Number: PCT/KR2004/000097

(22) International Filing Date: 20 January 2004 (20.01.2004)

(25) Filing Language: Korean

(26) Publication Language: English

(30) Priority Data:

10-2003-0004608	23 January 2003 (23.01.2003)	KR
10-2003-0004607	23 January 2003 (23.01.2003)	KR
10-2003-0042442	27 June 2003 (27.06.2003)	KR

(71) Applicants *(for all designated States except US)*: **CRYSTALGENOMICS, INC.** [KR/KR]; Biocommunity, #461-6, Jeonmin-dong, Yuseong-gu, Daejeon 305-390 (KR). **YUYU INC.** [KR/KR]; #212, Seoksu-1-dong, Manan-gu, Anyang-si, Kyungki-do 430-041 (KR).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **CHO, Joong Myung** [KR/KR]; Expo Apt. 509-401, Jeonmin-dong, Yuseong-gu, Daejeon 305-762 (KR). **RO, Seonggu** [KR/KR]; Expo Apt. 206-907, Jeonmin-dong, Yuseong-gu, Daejeon 305-761 (KR). **LEE, Tae Gyu** [KR/KR]; Expo Apt. 405-1504, Jeonmin-dong, Yuseong-gu, Daejeon 305-762 (KR). **LEE, Kyung Joo** [KR/KR]; Expo Apt. 206-1006, Jeonmin-dong, Yuseong-gu, Daejeon 305-761 (KR). **SHIN, Dongkyu** [KR/KR]; Daehung-203, 119-6 Sinsung-dong, Yusong-gu, Daejeon 305-804 (KR). **HYUN, Young-Lan** [KR/KR]; #302, 264-8, Jeonmin-dong, Yusung-gu, Daejeon 305-390 (KR). **LEE, Seung Chul** [KR/KR]; 57-2 Gajang-dong, Seogu, Daejeon 302-804 (KR). **KIM, Jin Hwan** [KR/KR]; Dule Apt. 108-108, Sinseong-dong, Yuseong-gu, Daejeon 305-345 (KR). **JEON, Young Ho** [KR/KR]; Hanul Apt. 105-506, Sinseong-dong, Yuseong-gu, Daejeon 305-345 (KR).

(74) Agents: **JANG, Seongku** et al.; 19th Fl., KEC Building, #275-7, Yangjae-dong, Seocho-ku, Seoul 137-130 (KR).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2004/065370 A1

(54) Title: GLYCOGEN SYNTHASE KINASE 3BETA INHIBITOR, COMPOSITION AND PROCESS FOR THE PREPARATION THEREOF

(57) Abstract: Novel compounds having hydroxybenzoimidazole carboxylic amide are useful for inhibiting glycogen synthase kinase 3β (GSK-3β).

GLYCOGEN SYNTHASE KINASE 3BETA INHIBITOR, COMPOSITION AND PROCESS FOR THE PREPARATION THEROF

Field of the Invention

The present invention relates to a compound for inhibiting glycogen synthase kinase 3beta (GSK-3β) activity, a pharmaceutical composition containing the compound as an active ingredient and a process for the preparation thereof.

Background of the Invention

Glycogen synthase kinase 3 (GSK-3), the well-known target protein for the treatment of diabetes and dementia, is a serine/threonine protein kinase which inhibits the activity of glycogen synthase (GS) by way of phosphorylation.

In the fatty tissue of mice suffering from fatty diabetes, the GSK-3β activity has been observed to be 2 fold higher than that of a normal mouse (H. Eldar-Finkelman, *Diabetes*, 48:1662-1666 (1999)) and patients during the second type diabetes are characterized by a high expression level of GSK-3β than normal (S. E. Nikoulina et al., *Diabetes*, 49: 263-171 (2000)). Also, the GSK-3β activity in the brain of a dementia patient is high (Yamaguchi H. et al., *Acta. N europathol.*, 92: 232-241 (1996)), and transgenic mice programmed to express GSK-3β in the brain have abnormal neurons caused by hyperphosphorylating tau of the neurofibrillary tangle which plays an important role in the dementia attack (Lucas J. J. et al., *EMBO J.* 20: 27-39 (2001)).

GSK-3β is further related to bipolar disorder which can be treated by lithium and valproic acid, well-known GSK-3β inhibitors (Elahi S. et al., *J. Infect. Dis.* 176: 217-226 (1997)).

Thus, there has existed a need to develop an effective inhibitor of GSK-3β for treating or preventing GSK-β-dependent diseases.

The present inventors have endeavored to develop an effective inhibitor of GSK-3β; and have unexpectedly found that a compound containing a hydroxybenzoimidazole carboxylic amide moiety can inhibit the activity of GSK-3β, and therefore, can be used for treating or preventing GSK-β-dependent diseases such as fatness, diabetes and dementia.

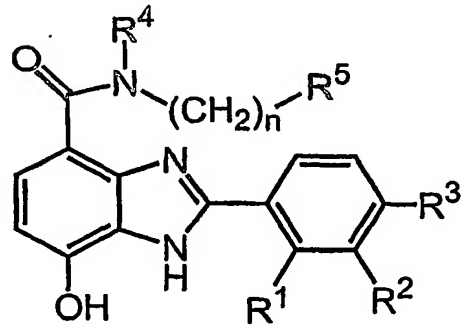
Summary of the Invention

Accordingly, it is an object of the present invention to provide a GSK-3β inhibitor having high inhibitory activity against GSK-3β .

It is another object of the present invention to provide a process for preparing said inhibitor.

It is further object of the present invention to provide a pharmaceutical composition for inhibiting GSK-3β .

In accordance with one aspect of the present invention, there is provided a compound of formula (I), a pharmaceutically acceptable salt, hydrate, solvate or isomer thereof:



I

wherein:

n is 0, 1, 2 or 3;

R^1, R^2 and R^3 are each independently hydrogen, hydroxy, halogen or morpholin-1-yl-ethylamino;

R^4 and R^5 are each independently hydrogen;

linear or cyclic C_1-C_6 alkyl optionally having one or more substituents, the carbon of the alkyl being optionally replaced with nitrogen, sulfur or oxygen, wherein the substituent is: hydroxy; halogen; alkyloxy; alkyl; amino; alkylamino; carboxyl; nitro; sulfonylamido; alkanesulfonyl; amido; an aromatic group optionally having one or more substituents selected from the group consisting of hydroxy, halogen, alkyloxy, alkyl, amino, alkylamino, carboxyl, nitro, amido, dioxoisoindole and sulfonylamino; an aromatic group having one or more substituents selected from the group consisting of hydroxy, halogen, alkyloxy, alkyl, amino, alkylamino, carboxyl, nitro and amido, the aromatic ring having nitrogen, sulfur or oxygen; or cyclic C_3-C_8 alkyl optionally having one or more

substituents selected from the group consisting of hydroxy, halogen, alkyloxy, alkyl, amino, alkylamino, carboxyl, nitro and amido;

an aromatic group optionally having one or more substituents, the aromatic ring having optional nitrogen, sulfur or oxygen, wherein the substituent is; hydroxy; halogen; alkyloxy; alkyl; amino; alkylamino; carboxyl; nitro; sulfonylamido, alkanesulfonyl; amido; or linear or cyclic C_1-C_6 alkyl optionally having one or more substituents, the alkyl having an optional nitrogen, sulfur or oxygen linkage and the substiuent of the alkyl being: hydroxy; halogen; alkyloxy; alkyl; amino; alkylamino; carboxyl; nitro; sulfonylamido, alkanesulfonyl; amido; an aromatic group optionally having one or more substituents selected from the group consisting of hydroxy; halogen; alkyloxy; alkyl; amino; alkylamino; carboxyl; nitro; amido; dioxoisoindole; and a sulfonylamino having an aromatic group substituted with hydroxy, halogen, alkyloxy, alkyl, amino, alkylamino, carboxyl, nitro, sulfonylamido, alkanesulfonyl or amido; an aromatic group optionally having one or more substituents selected form the group consisting of hydroxy, halogen, alkyloxy, alkyl, amino, alkylamino, carboxyl, nitro, sulfonylamide, alkanesulfonyl and amido, the aromatic ring containing nitrogen, sulfur or oxygen; or a cyclic C_3-C_8 alkyl optionally having one or more substituents selected from the group consisting of hydroxy, halogen, alkyloxy, alkyl, amino, alkylamino, carboxyl, nitro and amido; or

form, together with the $-N-(CH_2)_n-$ moiety to which they are attached, a nitrogen heterocycle optionally having one or more substituents selected from the group consisting of OH, NH_2, NO_2, the heterocycle containing optional nitrogen or oxygen.

Detailed Description of the Invention

Among the compounds of formula (I) of the present invention, the preferred are:

those wherein n, R^1, R^2 and R^3 have the same meaning as defined previously;

R^4 and R^5 are each independently hydrogen;

C_1-C_4 alkyl optionally having one or more substituents selected from the group consisting of OH, NH_2, NO_2, and an aromatic group, the aromatic group optionally having one or more substituents selected from the group consisting of OH, C_1-C_4 alkyloxy, NH_2, NO_2, methanesulfonylamino, ethanesulfonylamino, tolunensulfonylamino and dioxoisoindole; cyclic C_3-

C_8 alkyl optionally having one or more substituents selected from the group consisting of OH, NH_2 and NO_2; C_1-C_4 alkyl carrying a morpholine or oxopyrolidine group which is optionally substituted with OH, NH_2, NO_2 or -O-; C_1-C_4 alkyl or C_1-C_4 aminoalkyl carrying a pyrrol, pyrazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, isoxazole, oxazole, isotiazole, tiazolidine, tiazole, 1,2,5-oxadiazole, 1,2,3-oxadiazole, 1,2,5-thiodiazole, 1,2,3-thiodiazole, 1,3,4-oxadiazole, 1,3,4-thiodiazole, pyridine, pyrimidine or triazine group which is optionally having one or more substituents selected from the group consisting of Cl, OH, NH_2, NO_2, C_1-C_4 and phenyl;

cyclic C_3-C_8 alkyl optionally having one or more substituents selected from the group consisting of OH, NH_2 and NO_2;

an aromatic group optionally having one or more substituents selected from the group consisting of OH; NH_2; hydroxyalkyl; aminoalkyl; NO_2; and a C_1-C_4 alkyl group optionally having one or more substituents selected from the group consisting of OH, NH_2, NO_2, methanesulfonylamino, ethanesulfonylamino, tolunensulfonylamino, dioxoisoindole and thiophensulfonylamino; or

form, together with the -N-$(CH_2)_n$- moiety to which they are attached, a nitrogen heterocycle optionally having one or more substituents selected from the group consisting of OH, NH_2 and NO_2, the heterocycle containing 1 to 3 nitrogen, sulfur or oxygen atom.

In the present invention, the compounds of formula (I) as the below are most preferred:

those wherein n, R^1, R^2 and R^3 have the same meaning as defined previously; R^4 and R^5 are each independently hydrogen;

C_1-C_4 alkyl optionally having one or more substituents selected from the group consisting of OH, NH_2, NO_2, morpholine, nitropyridineamino, pyridine, oxopyrolidin, imidazole optionally having a Cl, CH_3 or phenyl substituent; and phenyl optionally having one or more substituents selected from the group consisting of OH, NH_2, methoxy, NO_2, methanesulfonylamino, ethanesulfonylamino, tolunensulfonylamino and dioxoisoindole;

cyclic C_3-C_8 alkyl optionally having one or more substituents selected from the group consisting of OH, NH_2 and NO_2;

phenyl optionally having one or more substituents selected from the group consisting of OH; NH_2; NO_2; and C_1-C_4 alkyl optionally having a OH,

NH_2, NO_2, methanesulfonylamino, ethanesulfonylamino, tolunensulfonylamino, dioxoisoindole or thiophensulfonylamino substituent; or

form, together with -N-$(CH_2)_n$- moiety to which they are attached, a piperidine ring optionally having one or more substituents selected from the group consisting of OH, NH_2 and NO_2.

Important compounds of the present invention are listed in Table 1 below.

Table 1

Com No.	n	R^1	R^2	R^3	R^4	R^5
1	0	H	H	H	H	H
2	0	H	H	H	H	Phenyl
3	0	H	H	H	H	4-hydroxyphenyl
4	0	H	H	H	H	4-aminophenyl
5	0	H	H	H	H	4-hydroxycyclohexyl
6	0	H	H	H	H	4-(hydroxymethyl)phenyl
7	0	H	H	H	H	4-(hydroxyethyl)phenyl
8	0	H	H	H	H	4-(aminoethyl)phenyl
9	0	H	H	H	H	4-(p-toluenesulfonamidylethyl)phenyl
10	0	H	H	H	H	4-(methanesulfonamidylethyl)phenyl
11	0	H	H	H	H	4-(phthalinidylethyl)phenyl
12	0	H	H	H	H	4-(2-thiophenylsulfonamidylethyl)phenyl
13	0	H	H	H	H	4-(ethansulfonamidylethyl)phenyl
14	0	H	H	Cl	H	phenyl
15	0	H	H	Cl	H	4-hydroxycyclohexyl

16	0	H	H	Cl	H	4-(p-toluenesulfonamidylethyl)phenyl
17	0	H	H	Cl	H	4-(methanesulfonamidylethyl)phenyl
18	0	H	H	Cl	H	4-(phthalinidylethyl)phenyl
19	0	H	H	Cl	H	4-(2-thiophenylsulfonamidylethyl)phenyl
20	0	H	H	Cl	H	4-(ethansulfonamidylethyl)phenyl
21	0	Cl	H	Cl	H	H
22	0	Cl	H	Cl	H	Phenyl
23	0	Cl	H	Cl	H	4-hydroxycyclohexyl
24	0	Cl	H	Cl	H	4-(aminoethyl)phenyl
25	0	Cl	H	Cl	H	4-aminophenyl
26	0	Cl	H	Cl	H	4-(hydroxymethyl)phenyl
27	0	Cl	H	Cl	H	4-(hydroxyethyl)phenyl
28	0	Cl	H	Cl	H	4-(p-toluenesulfonamidylethyl)phenyl
29	0	Cl	H	Cl	H	4-(methanesulfonamidylethyl)phenyl
30	0	Cl	H	Cl	H	4-(phthalinidylethyl)phenyl
31	0	Cl	H	Cl	H	4-(2-thiophenylsulfonamidylethyl)phenyl
32	0	Cl	H	Cl	H	4-(ethansulfonamidylethyl)phenyl
33	0	H	H	F	H	4-(methanesulfonamidylethyl)phenyl
34	0	H	H	F	H	4-(p-toluenesulfonamidylethyl)phenyl
35	0	H	H	F	H	4-(ethansulfonamidylethyl)phenyl
36	0	H	H	F	H	4-morpholinophenyl
37	0	F	H	F	H	4-(methanesulfonamidylethyl)phenyl
38	0	F	H	F	H	4-(p-toluenesulfonamidylethyl)phenyl

39	0	F	H	F	H	4-(ethansulfonamidylethyl)phenyl
40	0	Cl	H	F	H	4-(p-toluenesulfonamidylethyl)phenyl
41	0	Cl	H	F	H	4-(methanesulfonamidylethyl)phenyl
42	0	Cl	H	F	H	4-(ethansulfonamidylethyl)phenyl
43	0	H	Cl	F	H	4-(p-toluenesulfonamidylethyl)phenyl
44	0	H	Cl	F	H	4-(ethansulfonamidylethyl)phenyl
45	0	H	Cl	F	H	4-(methanesulfonamidylethyl)phenyl
46	0	H	H	H	R^4, R^5 = piperidinyl	
47	0	H	H	Cl	R^4, R^5 = piperidinyl	
48	0	Cl	H	Cl	R^4, R^5 = piperidinyl	
49	1	H	H	H	H	4-nitrophenyl
50	1	H	H	H	H	4-aminophenyl
51	1	H	H	H	H	phenyl
52	1	H	H	Cl	H	phenyl
53	1	H	H	Cl	H	4-nitrophenyl
54	1	H	H	Cl	H	4-aminophenyl
55	1	Cl	H	Cl	H	phenyl
56	1	Cl	H	Cl	H	4-nitrophenyl
57	2	H	H	H	H	phenyl
58	2	H	H	H	H	4-hydroxyphenyl
59	2	H	H	H	H	4-nitrophenyl
60	2	H	H	H	H	4-aminophenyl
61	2	H	H	H	H	amino

62	2	H	H	H	H	4-hydroxy-3-methoxyphenyl
63	2	H	H	H	H	3-hydroxy-4-methoxyphenyl
64	2	H	H	H	H	4-(methanesulfonamidyl)phenyl
65	2	H	H	H	H	4-(p-toluenesulfonamidyl)phenyl
66	2	H	H	H	H	4-morpholinyl
67	2	H	H	H	H	4-phthlimidophenyl
68	2	H	H	H	H	4-(ethanesulfonamidyl)phenyl
69	2	H	H	H	H	4-nitro-2-pyridinylamino
70	2	H	H	H	H	2-pyridyl
71	2	H	H	Cl	H	phenyl
72	2	H	H	Cl	H	4-nitrophenyl
73	2	H	H	Cl	H	4-aminophenyl
74	2	H	H	Cl	H	4-hydroxyphenyl
75	2	H	H	Cl	H	4-(methanesulfonamidyl)phenyl
76	2	H	H	Cl	H	4-(p-toluenesulfonamidyl)phenyl
77	2	H	H	Cl	H	3-hydroxy-4-methoxyphenyl
78	2	H	H	Cl	H	N-morpholinyl
79	2	H	H	Cl	H	4-phthalimidophenyl
80	2	H	H	Cl	H	4-(ethanesulfonamidyl)phenyl
81	2	H	H	Cl	H	4-nitro-2-pyridinylamino
82	2	H	H	Cl	H	2-pyridyl
83	2	H	H	Cl	H	4-imidazolyl
84	2	H	H	Cl	H	4-hydroxyphenyl

85	2	H	H	Cl	H	4-acetylamino-2-pyridylamino
86	2	H	H	Cl	H	4-(4-methylpiperazin-1-yl-acetylamino)phenyl
87	2	H	H	Cl	H	4-(4-ethylpiperazin-1-yl-acetylamino)phenyl
88	2	H	H	Cl	H	4-(dimethylaminoacetylamino)phenyl
89	2	H	H	Cl	H	4-(diethylaminoacetylamino)phenyl
90	2	H	H	Cl	H	4-aminophenyl
91	2	H	H	Cl	H	4-amino-2-pyridylamino
92	2	H	H	Cl	H	4-(morpholin-4-yl-acetylamino)phenyl
93	2	H	H	Cl	H	4-(*N*,*N*-dimethylamino)phenyl
94	2	H	H	Cl	H	4-(morpholin-4-yl-ethoxy)phenyl
95	2	H	H	Cl	H	4-(4-methylpiperazin-1-yl-ethoxy)phenyl
96	2	H	H	Cl	H	2-hydroxyphenyl
97	2	H	H	Cl	H	2-methoxyphenyl
98	2	H	H	Cl	H	3-bromophenyl
99	2	Cl	H	Cl	H	phenyl
100	2	Cl	H	Cl	H	4-nitrophenyl
101	2	Cl	H	Cl	H	4-hydroxy-3-methoxyphenyl
102	2	Cl	H	Cl	H	3-hydroxy-4-methoxyphenyl
103	2	Cl	H	Cl	H	amino
104	2	Cl	H	Cl	H	4-hydroxyphenyl
105	2	Cl	H	Cl	H	4-(p-toluenesulfonamidyl)phenyl
106	2	Cl	H	Cl	H	4-(methanesulfonamidyl)phenyl

107	2	Cl	H	Cl	H	4-phthlimidophenyl
108	2	Cl	H	Cl	H	4-morpholinyl
109	2	Cl	H	Cl	H	4-(ethanesulfonamidyl)phenyl
110	2	Cl	H	Cl	H	4-nitro-2-pyridinylamino
111	2	Cl	H	Cl	H	2-pyridyl
112	2	Cl	H	Cl	H	4-(acetylamino)phenyl
113	2	Cl	H	Cl	H	4-(pentanoylamino)phenyl
114	2	H	H	F	H	4-(methanesulfonamidyl)phenyl
115	2	H	H	F	H	4-(p-toluenesulfonamidyl)phenyl
116	2	H	H	F	H	4-(ethanesulfonamidyl)phenyl
117	2	H	H	F	H	4-(acetylamino)phenyl
118	2	H	H	F	H	4-methylpiperazin-1-yl
119	2	H	H	F	H	4-morpholin-1-yl
120	2	H	H	F	H	4-(pentanoylamino)phenyl
121	2	H	H	F	H	4-hydroxyphenyl
122	2	H	H	F	H	4-nitro-2-pyridinylamino
123	2	H	H	F	H	4-(methanesulfonylamino-2-pyridyl)amino
124	2	H	H	F	H	4-(p-toluenesulfonylamino-2-pyridyl)amino
125	2	H	H	F	H	4-imidazolyl
126	2	H	H	F	H	4-acetylamino-2-pyridylamino
127	2	H	H	F	H	4-(4-methylpiperazin-1-yl-acetylamino)phenyl
128	2	H	H	F	H	4-(4-ethylpiperazin-1-yl-acetylamino)phenyl

129	2	H	H	F	H	4-(dimethylaminoacetylamino)phenyl
130	2	H	H	F	H	4-(diethylaminoacetylamino)phenyl
131	2	H	H	F	H	4-aminophenyl
132	2	H	H	F	H	4-morpholinophenyl
133	2	H	H	F	H	4-(3-dimethylaminopyrrolidin-1-yl)phenyl
134	2	H	H	F	H	4-(morpholin-4-yl-acetylamino)phenyl
135	2	H	H	F	H	4-(N,N-dimethylamino)phenyl
136	2	H	H	F	H	4-(morpholin-4-yl-ethoxy)phenyl
137	2	H	H	F	H	2-hydroxyphenyl
138	2	H	H	F	H	2-methoxyphenyl
139	2	H	H	F	H	3-bromophenyl
140	2	F	H	F	H	4-(methanesulfonamidyl)phenyl
141	2	F	H	F	H	4-(p-toluenesulfonamidyl)phenyl
142	2	F	H	F	H	4-(ethanesulfonamidyl)phenyl
143	2	Cl	H	F	H	4-(methanesulfonamidyl)phenyl
144	2	Cl	H	F	H	4-(p-toluenesulfonamidyl)phenyl
145	2	Cl	H	F	H	4-(ethanesulfonamidyl)phenyl
146	2	Cl	H	F	H	4-(acetylamino)phenyl
147	2	Cl	H	F	H	4-morpholin-1-yl
148	2	Cl	H	F	H	4-methylpiperazin-1-yl
149	2	Cl	H	F	H	4-(pentanoylamino)phenyl
150	2	Cl	H	F	H	4-hydroxyphenyl
151	2	Cl	H	F	H	4-nitro-2-pyridinylamino

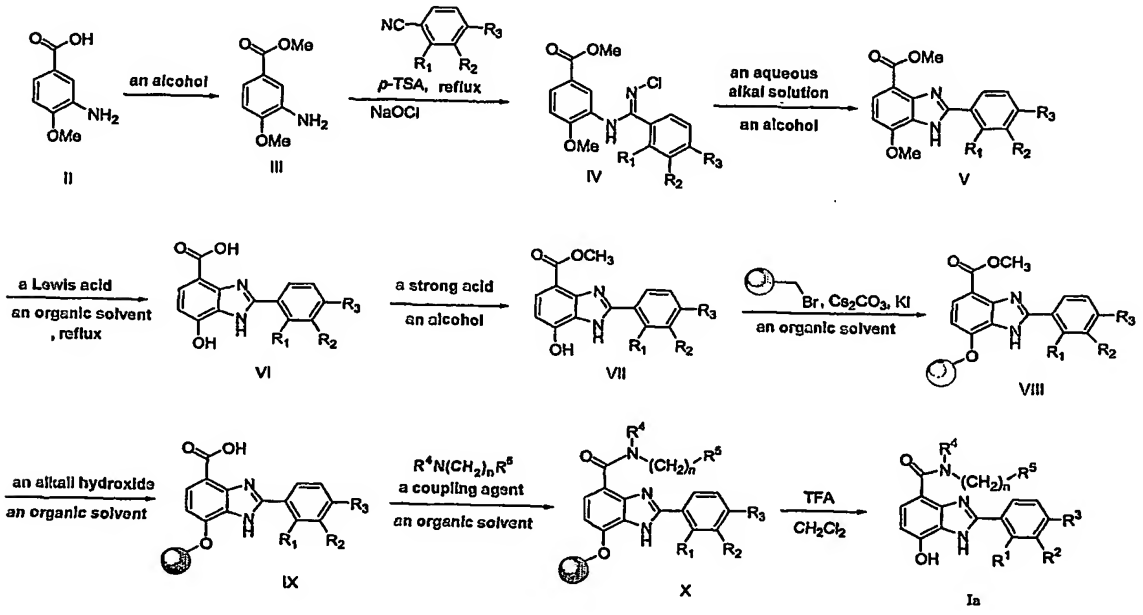
152	2	Cl	H	F	H	4-(methanesulfonylamino-2-pyridyl)amino
153	2	Cl	H	F	H	4-(p-toluenesulfonylamino-2-pyridyl)amino
154	2	Cl	H	F	H	4-imidazolyl
155	2	Cl	H	F	H	4-acetylamino-2-pyridylamino
156	2	Cl	H	F	H	4-(4-methylpiperazin-1-yl-acetylamino)phenyl
157	2	Cl	H	F	H	4-(4-ethylpiperazin-1-yl-acetylamino)phenyl
158	2	Cl	H	F	H	4-(dimethylaminoacetylamino)phenyl
159	2	Cl	H	F	H	4-(diethylaminoacetylamino)phenyl
160	2	H	Cl	F	H	4-(p-toluenesulfonamidyl)phenyl
161	2	H	Cl	F	H	4-(methanesulfonamidyl)phenyl
162	3	H	H	H	H	methyl
163	3	H	H	H	H	amino
164	3	H	H	H	H	2-oxopyrrolidin-1-yl
165	3	H	H	H	H	1-imidazolyl
166	3	H	H	H	H	4-N-morpholinyl
167	3	H	H	H	H	2-methylimidazol-1-yl
168	3	H	H	Cl	H	methyl
169	3	H	H	Cl	H	2-oxopyrrolidin-1-yl
170	3	H	H	Cl	H	1-imidazolyl
171	3	H	H	Cl	H	4-morpholinyl
172	3	H	H	Cl	H	2-phenylimidazol-1-yl
173	3	H	H	Cl	H	4-methylimidazol-1-yl

174	3	H	H	Cl	H	4,5-dichloroimidazol-1-yl
175	3	H	H	Cl	H	2-methylimidazol-1-yl
176	3	Cl	H	Cl	H	methyl
177	3	Cl	H	Cl	H	2-oxopyrrolidin-1-yl
178	3	Cl	H	Cl	H	1-imidazolyl
179	3	Cl	H	Cl	H	4-morpholin-yl
180	3	Cl	H	Cl	H	2-phenylimidazol-1-yl
181	3	Cl	H	Cl	H	4-methylimidazol-1-yl
182	3	Cl	H	Cl	H	4,5-dichloroimidazol-1-yl
183	3	Cl	H	Cl	H	2-methylimidazol-1-yl
184	3	Cl	H	Cl	H	2-isopropylimidazol-1-yl
185	3	H	H	F	H	1-imidazolyl
186	3	H	H	F	H	2-isopropylimidazol-1-yl
187	3	H	H	F	H	4-methylimidazol-1-yl
188	3	H	H	F	H	2-methylimidazol-1-yl
189	3	H	H	F	H	2-ethylimidazol-1-yl
190	3	H	H	F	H	4,5-dichloroimidazol-1-yl
191	3	F	H	F	H	2-isopropylimidazol-1-yl
192	3	F	H	F	H	1-imidazolyl
193	3	F	H	F	H	4-methylimidazol-1-yl
194	3	F	H	F	H	4,5-dichloroimidazol-1-yl
195	3	F	H	F	H	2-methylimidazol-1-yl
196	3	F	H	F	H	2-ethylimidazol-1-yl

197	3	F	H	F	H	4,5-dichloroimidazol-1-yl
198	3	Cl	H	F	H	1-imidazolyl
199	3	Cl	H	F	H	4-methylimidazol-1-yl
200	3	Cl	H	F	H	4,5-dichloroimidazol-1-yl
201	3	Cl	H	F	H	2-methylimidazol-1-yl
202	3	H	Cl	F	H	4-methylimidazol-1-yl
203	3	H	Cl	F	H	1-imidazolyl
204	3	R^1, R^2 and R^4 = H R^3 = morpholin-1-yl-ethylamino				4,5-dichloroimidazol-1-yl

The inventive compound (except for the compound wherein R^3 is morpholin-1-yl-ethylamino) of formula (Ia) may be prepared as in Scheme 1.

Scheme I

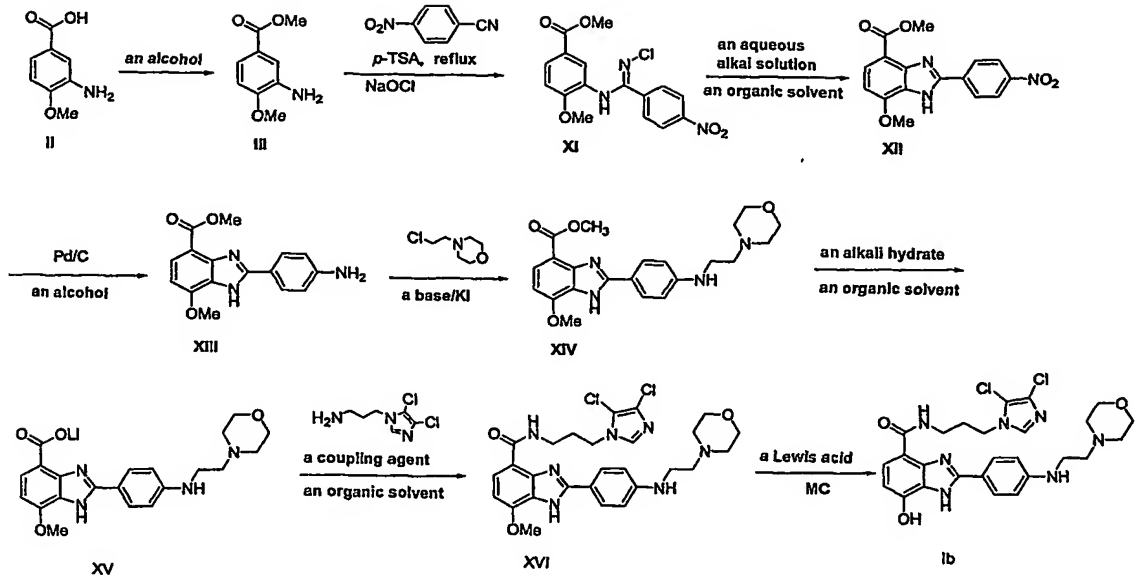


wherein, *p*-TSA is *p*-toluenesulfonic acid, DMF is dimethylformamide, THF is tetrahydrofuran, TFA is trifluoroacetic acid, EDCI is ethyl-dimethylaminopropyl-carbodiimide hyrochloride, DMAP is 4-dimethylaminoprydine, HOBt is N-hydroxybezotriazole, n, R^1, R^2, R^3, R^4 and R^5 have the same meaning as defined previously.

As shown in Scheme I, the compound of formula (Ia) can be prepared by reacting 3-amino-4-methoxy benzoic acid (compound II) and an alcohol (e.g., methanol or ethanol) to obtain compound (III); adding anhydrous *p*-toluenesulfonic acid and benzonitrile to the compound (III) thus obtained, refluxing the mixture at 80 to 200 ℃, adding NaOCl thereto at room temperature and purifying by silica gel column chromatography to obtain compound (IV); dissolving the compound (IV) thus obtained in an alcohol (e.g., methanol or ethanol), adding an aqueous alkali solution (Na_2CO_3, $NaHCO_3$, K_2CO_2 or $KHCO_3$ solution) thereto and refluxing the mixture to obtain compound (V); dissolving the compound (V) thus obtained in an organic solvent, e.g., toluene, adding a Lewis acid (e.g., $AlCl_3$ or BBr_3) thereto and refluxing the mixture to obtain compound (VI); dissolving the compound (V) thus obtained in an alcohol, adding a strong acid, nitric acid or sulfuric acid, thereto at room temperature and refluxing the mixture to obtain compound (VII); dissolving the compound (VII) thus obtained and (4-bromomethylphenoxy)-methyl polystyrene Wang resin in an organic solvent, e.g., DMF, THF or chloroform, adding a base ($CsCO_3$, Na_2CO_3, $NaHCO_3$, K_2CO_3 or $KHCO_3$) and KI thereto (1:3:3:3) and stirring the mixture at 50 to 60 ℃ for 1 to 24 hours to obtain compound (VIII); dissolving the compound (VIII) thus obtained in an organic solvent, adding an alcohol solution of an alkali hydroxide (e.g., LiOH, NaOH or KOH) thereto and refluxing the mixture to obtain compound (IX); dissolving the compound (IX) thus obtained in an organic solvent, adding $R^4N(CH_2)_nR^5$ and a coupling agent (e.g., EDCI/DMAP/HOBt, DCC or pyBop) thereto and stirring the mixture at room temperature to obtain compound (X); and dissolving the compound (X) thus obtained in CH_2Cl_2, adding trifluoroacetic acid thereto and stirring the mixture at room temperature to obtain compound (Ia).

The inventive compound (wherein R^3 is morpholin-1-yl-ethylamino) represented to formula (Ib) may be prepared, as in Scheme II.

Scheme II



As shown in Scheme II, the compound of formula (Ib) can be prepared by reacting 3-amino-4-methoxy benzoic acid (compound II) and an alcohol (e.g., methanol or ethanol) to obtain compound (III), adding *p*-toluenesulfonic acid, benzene and 4-nitrobezonitrile thereto, refluxing the mixture at 80 to 200 ℃, adding NaOCl thereto at room temperature and purifying by silica gel column chromatography to obtain compound (XI); dissolving the compound (XI) thus obtained in an organic solvent, adding an aqueous alkali solution (e.g., Na_2CO_3 solution) thereto, refluxing the mixture and purifying by silica gel column chromatography to obtain compound (XII); dissolving the compound (XII) thus obtained in an alcohol, adding Pd/C thereto and refluxing the mixture to obtain compound (XIII); dissolving the compound (XIII) thus obtained in an organic solvent, adding a base (e.g., $CsCO_3$, Na_2CO_3, $NaHCO_3$, K_2CO_3 or $KHCO_3$), 2-chloroethylmorphine and potassium iodide thereto and stirring the mixture at room temperature to obtain compound (XIV); dissolving the compound (XIV) obtained thus in an organic solvent, adding an alkali hydrate, stirring the mixture at room temperature to obtain compound (XV); dissolving the compound (XV) thus obtained in an organic solvent, adding 4,5-dichloro-1-(3-aminoprophyl)imidazole and a coupling agent (e.g., EDCI, DMAP or HOBt), stirring the mixture at room temperature and purifying by silica gel

column chromatography to obtain compound (XVI); and dissolving the compound (XVI) thus obtained in MC, adding a Lewis acid thereto, stirring the mixture, concentrating the resulting solution under a reduced pressure and purifying by silica gel column chromatography to obtain compound (Ib).

A salt, hydrate, solvate and isomer of the inventive compound of formula (I) may be prepared by employing any of the known methods. The inventive compound of formula (I), a salt, hydrate, solvate or isomer thereof may used for the treatment of GSK-3β-dependent diseases including fatness, diabetes and dementia, by way of inhibiting GSK-3β activity, the inventive compound having an IC_{50} value in the range of 1 to 10,000 nM.

Accordingly, the present invention includes a pharmaceutical composition which comprises a therapeutically effective amount of the compound of formula (I), a salt, hydrate, solvate or isomer thereof as an active ingredient and a pharmaceutically acceptable carrier; therefore, the pharmaceutical composition of the present invention exerts superior preventive and treating effects on GSK-β-dependent diseases such as fatness, diabetes and dementia and the like.

A pharmaceutical formulation may be prepared in accordance with any of the conventional procedures. In preparing the formulation, the active ingredient is preferably admixed or diluted with a carrier, or enclosed within a carrier, sachet or other container. When the carrier serves as a diluent, it may be a solid, semi-solid or liquid material acting as a vehicle, excipient or medium for the active ingredient. Thus, the formulations may be in the form of a tablet, pill, powder, sachet, elixir, suspension, emulsion, solution, syrup, aerosol, soft and hard gelatin capsule, sterile injectable solution, sterile packaged powder and the like.

Examples of suitable carriers, excipients, and diluents are lactose, dextrose, sucrose, sorbitol, mannitol, calcium silicate, cellulose, methyl cellulose, microcrystalline cellulose, polyvinylpyrrolidone, water, methylhydroxybenzoates, propylhydroxybenzoates, talc, magnesium stearate and mineral oil. The formulations may additionally include fillers, anti-agglutinating agents, lubricating agents, wetting agents, flavoring agents, emulsifiers, preservatives and the like. The compositions of the invention may be formulated so as to provide quick, sustained or delayed release of the active ingredient after their administration to a mammal by employing any of the procedures well known in the art.

The pharmaceutical composition of the present invention can be administered via various routes including oral, transdermal, subcutaneous, intravenous and intramuscular introduction. In case of human, a typical daily dose of the compound of formula (I) may range from about 0.01 to 100 mg/kg body weight, preferably 0.1 to 50 mg/kg body weight, and can be administered in a single dose or in divided doses. However, it should be understood that the amount of the active ingredient actually administered ought to be determined in light of various relevant factors including the condition to be treated, the chosen route of administration, the age, sex and body weight of the individual patient, and the severity of the patient's symptom; and, therefore, the above dose should not be intended to limit the scope of the invention in any way.

The following examples are intended to further illustrate the present invention without limiting its scope.

Preparation Example 1: Preparation of Wang resin (*p*-benzyloxybenzyl alcohol resin)-supported 7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid (R^1 = H, R^2 = H and R^3 = H)

(1) Preparation of 3-amino-4-methoxy benzoic acid methyl ester

3-amino-4-methoxy benzoic acid (40 g, 0.239 mol) was dissolved in methanol, H_2SO_4 (38.14 ml, 0.717 mol) was added dropwise thereto and refluxed for 12 hours. The resulting mixture was cooled to room temperature and concentrated under a reduced pressure to remove methanol, neutralized with $NaHCO_3$, extracted with ethyl acetate, and the extract was concentrated under a reduced pressure. The resulting residue was purified by recrystallization from ethyl acetate/hexane to obtain the title compound (39 g, 0.215 mol) in a yield of 90 %.

^{1}H NMR ($CDCl_3$): δ 7.87-7.78 (2H, m), 7.22 (1H, d), 3.93 (3H, s), 3.82 (3H, s)

MW: 181

(2) Preparation of 4-methoxy-3-[(*N*-chloro-benzimidoyl)-amino]-benzoic acid methyl ester

Anhydrous *p*-toluene sulfonic acid (41.99 g, 220.8 mmol) was melted at 120 ℃ and 3-amino-4-methoxy benzoic acid methyl ester (20 g, 110.38 mmol) obtained in step 1 and benzonitrile (22.77 g, 220.8 mmol) were added thereto and stirred at 180 ℃ for 5 hours. The resulting solution was cooled to room temperature and the reaction was stopped by adding $NaHCO_3$ thereto. The resulting mixture was extracted with ethyl acetate, the extract was dried over $MgSO_4$ and concentrated under a reduced pressure. The concentrate was dissolved in 50% methanol and 5% NaOCl (56 ml, 37.65 mmol) was added dropwise thereto. After 5 min, the resulting mixture was extracted with ethyl acetate, the extract was dried over $MgSO_4$ and concentrated under a reduced pressure. The resulting residue was purified by silica gel column chlomatography (eluent – MeOH/$CDCl_3$ = 5 : 95, Merck, Silicagel 60) to obtain the title compound (31 g, 25.10 mmol) in a yield of 88%.

^{1}H NMR ($CDCl_3$): δ 7.78 (1H, d), 7.48(1H, s), 7.37-7.24 (5H, m), 6.95 (1H, d), 3.78 (6H, s)

MW : 318

(3) Preparation of 7-methoxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid methyl ester

4-methoxy-3-[(*N*-chloro-benzimidoyl)-amino]-benzoic acid methyl ester (8 g, 25.10 mmol) obtained in step 1 was dissolved in 50 ml of 50% methanol and $NaHCO_3$ (5.32 g, 50.20 mmol) was added dropwise thereto at room temperature and refluxed for 5 min. The resulting solution was cooled to room temperature, extracted with ethyl acetate, and the extract was concentrated under a reduced pressure. The resulting residue was purified by recrystallization from ethyl acetate/hexane to obtain the title compound (6 g, 15.94 mmol) in a yield of 86 %.

^{1}H NMR ($CDCl_3$): δ 10.65 (1H, br), 8.23 (2H, d), 7.49 (3H, m), 6.75 (1H, d), 4.13 (3H, s), 3.99 (3H, s)

MW : 282

(4) Preparation of 7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid

7-methoxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid methyl ester (4.5 g, 15.94 mmol) obtained in step 3 was dissolved in 100 ml of toluene, aluminum chloride (9.56 g, 71.73 mmol) was added thereto and refluxed for 8 hours. The resulting solution was cooled to room temperature, the reaction was stopped by adding 3 N HCl thereto and stirred for 30 min. The precipitate formed was filtered, washed with benzene and dried to obtain the title compound (3.5 g, 13.77 mmol) in a yield of 86%.

^{1}H NMR (DMSO-d_6): δ 8.29 (2H, d), 7.68 (1H, d), 7.56-7.49 (3H, m), 6.67 (1H, d)

MW : 254

(5) Preparation of 7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid methyl ester

7-methoxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid (2.00 g, 7.46 mmol) obtained in step 4 was dissolved in 30 ml of methanol, H_2SO_4 (2.00 ml, 37.28 mmol) was added dropwise thereto and refluxed for 15 hours. The resulting solution was cooled to room temperature, concentrated under a reduced pressure to remove methanol, and the residue was neutralized with $NaHCO_3$. Then, the neutralized residue was extracted with ethyl acetate and concentrated under a reduced pressure to obtain a residue which purified by recrystallization from $CHCl_3$/MeOH/hexane to obtain the title compound (1.7 g, 5.89 mmol) in a yield of 83 %.

^{1}H NMR (CH_3OH-d_4): δ 7.82 (1H, d), 7.42-7.25 (5H, m), 6.64 (1H, d), 4.92 (3H, s)

MW : 268

(6) Preparation of Wang resin (*p*-benzyloxybenzyl alcohol resin)-supported 7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid methyl ester

p-nitrophenyl carbonate Wang resin (476 mg, 0.67 mmol) was dissolved in DMF, and 7-hydroxy-2-phenyl-1H-benzoimidazole-4-

carboxylic acid methyl ester (567 ㎎, 2.01 mmol) obtained in step 5, Cs_2CO_3 (655 ㎎, 2.01 mmol) and KI (334 ㎎, 2.01 mmol) were added thereto to be stirred at 50 to 60 ℃ for 12 hours. The resulting solution was cooled to room temperature and filtered. The filtrate was washed with DMF, MeOH and CH_2Cl_2 and dried to obtain the title compound (608 mg, 0.65 mmol) in a yield of 98 %.

(7) Preparation of Wang resin-supported 7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid methyl ester

Wang resin-supported 7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid methyl ester (570 ㎎, 0.47 mmol) obtained in step 6 was dissolved in THF, $LiOH{\cdot}H_2O$ (99 ㎎, 2.35 mmol) in MeOH-H_2O (2 : 1) was added thereto and refluxed for 5 hours. The resulting solution was cooled to room temperature and filtered. The filtrate was washed with MeOH and CH_2Cl_2, and dried to obtain the title compound (551 mg, 0.42 mmol) in a yield of 90 %.

Preparation Example 2: Preparation of 2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (R^1 = H, R^2 = H and R^3 = Cl)

(1) Preparation of 3-[(4-chloro-N-chloro-benzimidoyl)-amino]-4-methoxy-benzoic acid methyl ester

Anhydrous *p*-toluene sulfonic acid (41.99 g, 220.76 mmol) was melted at 120 ℃ and 3-amino-4-methoxy benzoic acid methyl ester (20 g, 110.38 mmol) obtained in step 1 of Preparation Example 1 and 4-chlorobenzonitrile (22.78 g, 165.57 mol) were added thereto and stirred at 160 ℃ for 8 hours. The resulting solution was cooled to room temperature and the reaction was stopped by adding 1M $NaHCO_3$ thereto. The resulting mixture was extracted with ethyl acetate, the extract was dried over $MgSO_4$ and concentrated under a reduced pressure. The concentrate was dissolved in 500 ml of 50% methanol and 5% NaOCl (197 ㎖, 132.46 mmol) was added dropwise thereto. After 5 min, the resulting mixture was extracted with ethyl acetate, the extract was dried over $MgSO_4$ and concentrated under a reduced pressure. The resulting residue was purified by silica gel column chlomatography (eluent – MeOH : $CDCl_3$ = 5 : 95,

Merck, Silicagel 60) to obtain the title compound (19.43 g, 55.19 mmol) in a yield of 50%.

^{1}H NMR (CH_3OH-d_4): δ 7.62 (2H, m), 7.22-7.15 (4H, m), 6.59 (1H, s), 4.00-3.80 (6H, d)
MW : 352

(2) Preparation of 2-(4-chloro-phenyl)-7-methoxy-1H-benzoimidazole-4-carboxylic acid methyl ester

3-[(4-chloro-N-chloro-benzimidoyl)-amino]-4-methoxy-benzoic acid methyl ester (5.5 g, 15.63 mmol) obtained in step 1 was dissolved in 40 ml of 50% methanol and Na_2CO_3 (3.53 g, 33.26 mmol) was added dropwise thereto at room temperature and refluxed for 5 min. The resulting solution was cooled to room temperature, extracted with ethyl acetate, the extract was concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography to obtain the title compound (2.57 g, 8.13 mmol) in a yield of 52 %.

^{1}H NMR ($CDCl_3$): δ 8.15 (2H, d), 7.95 (1H, d), 7.51 (2H, m), 6.75 (1H, d), 4.06 (3H, s)
MW : 316

(3) Preparation of 2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid

2-(4-chloro-phenyl)-7-methoxy-1H-benzoimidazole-4-carboxylic acid methyl ester (1.0 g, 3.16 mmol) obtained in step 2 was dissolved in 10 ml of toluene, aluminum chloride (2.11 g, 15.8 mmol) was added thereto and refluxed for 8 hours. The resulting solution was cooled to room temperature, the reaction was stopped by adding 3 N HCl thereto and stirred for 30 min. The precipitate formed was filtered, washed with benzene and dried to obtain the title compound (745 mg, 2.59 mmol) in a yield of 82%.

^{1}H NMR (CH_3OH-d_4): δ 8.06 (3H, m), 7.50 (2H, m), 6.97 (1H, d)
MW : 288

(4) Preparation of 2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid methyl ester

2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (200 mg, 0.69 mmol) obtained in step 3 was dissolved in 5 ml of methanol, H_2SO_4 (0.18 ml, 3.45 mmol) was added dropwise thereto and refluxed for 15 hours. The resulting solution was cooled to room temperature, concentrated under a reduced pressure to remove methanol, and the residue was neutralized with 1M $NaHCO_3$. Then, the neutralized residue was extracted with ethyl acetate and concentrated under a reduced pressure to obtain a residue which was purified by silica gel column chromatography (eluent – MeOH / $CDCl_3$ = 5 / 95, Merck, Silicagel 60) to obtain the title compound (166 mg, 0.55 mmol) in a yield of 80 %.

^1H NMR (CH_3OH-d_4): δ 10.75 (1H, Br), 7.89 (3H, m), 7.46 (2H, d), 6.82 (1H, d), 3.39 (3H, s)

MW : 302

(5) Preparation of Wang resin-supported 2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid methyl ester

(4-bromomethylphenoxy)-methyl polystyrene Wang resin (476 ㎎, 0.67 mmol) was dissolved in 5 ml of DMF, and 2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid methyl ester (567 ㎎, 2.01 mmol) obtained in step 4, Cs_2CO_3 (655 ㎎, 2.01 mmol) and KI (334 ㎎, 2.01 mmol) were added thereto to be stirred at 50 to 60 ℃ for 12 hours. The resulting solution was cooled to room temperature and filtered. The filtrate was washed with DMF, MeOH and CH_2Cl_2 and dried to obtain the title compound (608 mg, 0.65 mmol) in a yield of 98 %.

(6) Preparation of Wang resin-supported 2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid

Wang resin-supported 2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid methyl ester (570 ㎎, 0.47 mmol) obtained in step 5 was dissolved in THF, $LiOH{\cdot}H_2O$ (99 ㎎, 2.35 mmol) in MeOH-H_2O (1 : 1) was added thereto and the resulting mixture was refluxed

for 5 hours. The resulting solution was cooled to room temperature and filtered. The filtrate was washed with MeOH and CH_2Cl_2, and dried to obtain the title compound (551 mg, 0.42 mmol) in a yield of 90 %.

Preparation Example 3: Preparation of 2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (R^1 = Cl, R^2 = H and R^3 = Cl)

(1) Preparation of 3-[(2,4-dichloro-*N*-chloro-benzimidoyl)-amino]-4-methoxy-benzoic acid methyl ester

Anhydrous *p*-toluene sulfonic acid (20.99 g, 110.04 mmol) was melted at 120 ℃ and 3-amino-4-methoxy benzoic acid methyl ester (10 g, 55.20 mmol) obtained in step 1 of Preparation Example 1 and 2,4-dichlorobenzonitrile (18.99 g, 110.04 mol) were added thereto and stirred at 180 ℃ for 6 hours. The resulting solution was cooled to room temperature and the reaction was stopped by adding $NaHCO_3$ thereto. The resulting mixture was extracted with ethyl acetate, the extract was dried over $MgSO_4$ and concentrated under a reduced pressure. The concentrate was dissolved in 50% methanol and 5% NaOCl (30 mℓ, 20.64 mmol) was added dropwise thereto. After 5 min, the resulting mixture was extracted with ethyl acetate, the extract was dried over $MgSO_4$ and concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography (eluent – MeOH : $CDCl_3$ = 5 : 95, Merck, Silicagel 60) to obtain the title compound (18 g, 10.32 mmol) in a yield of 84%.

^{1}H NMR ($CDCl_3$): δ 8.23 (1H, br), 7.75 (1H, d), 7.44 (1H, d), 7.36-7.26 (2H, m), 7.03 (1H, s), 6.88 (1H, d), 3.96 (3H, s), 3.76 (3H, s)
MW : 318

(2) Preparation of 2-(2,4-dichloro-phenyl)-7-methoxy-1H-benzoimidazole-4-carboxylic acid methyl ester

3-[(2,4-dichloro-*N*-chloro-benzimidoyl)-amino]-4-methoxy-benzoic acid methyl ester (4 g, 10.32 mmol) obtained in step 1 was dissolved in 50 ml of 50% methanol and $NaHCO_3$ (2.19 g, 20.64 mmol) was added dropwise thereto at room temperature and refluxed for 5 min. The resulting solution was cooled to room temperature, extracted with ethyl acetate, and the extract

was concentrated under a reduced pressure. The resulting residue was purified by recrystallization from ethyl acetate/hexane to obtain the title compound (3.2 g, 5.47 mmol) in a yield of 88 %.

^{1}H NMR ($CDCl_3$): δ 8.54 (1H, d), 7.94 (1H, d), 7.48 (1H, s), 7.42 (1H, d), 6.76 (1H,d), 4.44 (3H, s), 3.99 (3H, s)
MW : 351

(3) Preparation of 2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid

2-(2,4-dichloro-phenyl)-7-methoxy-1H-benzoimidazole-4-carboxylic acid methyl ester (1.9 g, 5.47 mmol) obtained in step 2 was dissolved in 100 ml of toluene, aluminum chloride (3.61 g, 27.05 mmol) was added thereto and refluxed for 8 hours. The resulting solution was cooled to room temperature, the reaction was stopped by adding 3 N HCl thereto and stirred for 30 min. The precipitate formed was filtered, washed with benzene and dried to obtain the title compound (1.63 g, 5.03 mmol) in a yield of 92%.

^{1}H NMR (DMSO-d_6): δ 8.19 (1H, d), 7.78 (1H, d), 7.62-7.55 (2H, m), 6.82 (1H, d)
MW : 323

(4) Preparation of 2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid methyl ester

2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (1.63 g, 5.03 mmol) obtained in step 3 was dissolved in 30 ml of methanol, and H_2SO_4 (1.08 ml, 20.12 mmol) was added dropwise thereto and refluxed for 15 hours. The resulting solution was cooled to room temperature, concentrated under a reduced pressure to remove methanol, and the residue was neutralized with $NaHCO_3$. Then, the neutralized residue was extracted with ethyl acetate and concentrated under a reduced pressure to obtain a residue which was purified by recrystallization from ethyl acetate/hexane to obtain the title compound (1.5 g, 3.62 mmol) in a yield of 86 %.

^{1}H NMR ($CDCl_3$): δ 11.42 (1H, br), 8.21 (1H, d), 7.89 (1H, d), 7.56 (1H, s), 7.38 (1H, d), 6.82 (1H, d), 3.99 (3H, s)
MW : 337

(5) Preparation of Wang resin-supported 2-(2,4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid methyl ester

p-nitrophenyl carbonate Wang resin (476 ㎎, 0.67 mmol) was dissolved in DMF, and 2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid methyl ester (567 ㎎, 2.01 mmol), obtained in step 4, Cs_2CO_3 (655 ㎎, 2.01 mmol) and KI (334 ㎎, 2.01 mmol) were added thereto to be stirred at 50 to 60 ℃ for 12 hours. The resulting solution was cooled to room temperature and filtered. The filtrate was washed with DMF, MeOH and CH_2Cl_2 and dried to obtain the title compound (608 mg, 0.65 mmol) in a yield of 98 %.

(6) Preparation of Wang resin-supported 2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid

Wang resin-supported 2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid methyl ester (570 ㎎, 0.47 mmol) obtained in step 5 was dissolved in THF, $LiOH{\cdot}H_2O$ (99 ㎎, 2.35 mmol) in MeOH-H_2O (2 : 1) was added thereto and the resulting mixture was refluxed for 5 hours. The resulting solution was cooled to room temperature and filtered. The filtrate was washed with MeOH and CH_2Cl_2, and dried to obtain the title compound (551 mg, 0.42 mmol) in a yield of 90 %.

Preparation Example 4: Preparation of Wang resin-supported 2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (R^1 = H, R^2 = H and R^3 = F)

(1) Preparation of 3-[(4-fluoro-benzimidoyl)-amino]-4-methoxy-benzoic acid methyl ester

Anhydrous *p*-toluene sulfonic acid (41.99 g, 220.76 mmol) was melted at 120 ℃ and 3-amino-4-methoxy benzoic acid methyl ester (20 g, 110.38 mmol) obtained in step 1 of Preparation Example 1 and 4-

fluorobenzonitrile (20.00 g, 165.57 mol) were added thereto and stirred at 160 ℃ for 8 hours. The resulting solution was cooled to room temperature and the reaction was stopped by adding $NaHCO_3$ thereto. The resulting mixture was extracted with ethyl acetate, the extract was dried over $MgSO_4$ and concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography (eluent – MeOH : $CDCl_3$ = 5 : 95, Merck, Silicagel 60) to obtain the title compound (22.67 g, 75.06 mmol) in a yield of 68%.

^1H NMR ($CDCl_3$): δ 7.92-7.75 (4H, m), 7.15-7.02 (3H, m), 3.87-3.81 (6H, d)
MW : 302

(2) Preparation of 2-(4-fluoro-phenyl)-7-methoxy-1H-benzoimidazole-4-carboxylic acid methyl ester

3-[(4-fluoro-benzimidoyl)-amino]-4-methoxy-benzoic acid methyl ester (10 g, 34.48 mmol) obtained in step 1 was dissolved in 50% methanol and 5% NaOCl (61 ml, 41.38 mmol) was added dropwise thereto at room temperature. After 5 min, Na_2CO_3 (7.31 g, 68.96 mmol) was added dropwise thereto and refluxed for 5 min. The resulting solution was cooled to room temperature, extracted with ethyl acetate, and the extract was concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography to obtain the title compound (5.66 g, 19.65 mmol) in a yield of 57 %.

^1H NMR ($CDCl_3$): δ 8.18 (2H, t), 7.91 (1H, d), 7.30-7.25 (2H, t), 6.65 (1H, d), 6.85 (1H, d), 4.08 (3H, s), 3.98 (3H, s)
MW : 300

(3) Preparation of 2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid

2-(4-fluoro-phenyl)-7-methoxy-1H-benzoimidazole-4-carboxylic acid methyl ester (3 g, 10.00 mmol) obtained in step 2 was dissolved in toluene, aluminum chloride (6.67 g, 30.00 mmol) was added thereto and refluxed for 8 hours. The resulting solution was cooled to room

temperature, the reaction was stopped by adding 3 N HCl thereto and stirred for 30 min. The precipitate formed was filtered, washed with benzene and dried to obtain the title compound (1.96 g, 7.20 mmol) in a yield of 72%.

^{1}H NMR (MeOH-d_4): δ 8.19-8.15 (2H, t), 8.06 (1H, d), 7.50-7.44 (2H, t), 7.00 (1H, d)

MW : 272

(4) Preparation of 2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid methyl ester

2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (500 mg, 1.84 mmol) obtained in step 3 was dissolved in methanol, H_2SO_4 (0.49 ml, 9.20 mmol) was added dropwise thereto and refluxed for 15 hours. The resulting solution was cooled to room temperature, concentrated under a reduced pressure to remove methanol, and the residue was neutralized with $NaHCO_3$. Then, the neutralized residue was extracted with ethyl acetate and concentrated under a reduced pressure to obtain a residue which was purified by silica gel chromatography to obtain the title compound (397 mg, 1.39 mmol) in a yield of 76 %.

^{1}H NMR (CH_3OH-d_4): δ 8.22-8.18 (2H, t), 7.80 (1H, d), 7.32-7.26 (2H, t), 6.70 (1H, d), 3.97 (3H, s)

MW : 286

(5) Preparation of Wang resin-supported 2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid methyl ester

(4-bromomethylphenoxy)-methyl polystyrene Wang resin (476 mg, 0.67 mmol) was dissolved in DMF, and 2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid methyl ester (567 mg, 2.01 mmol) obtained in step 4, Cs_2CO_3 (655 mg, 2.01 mmol) and KI (334 mg, 2.01 mmol) were added thereto to be stirred at 50 to 60 ℃ for 12 hours. The resulting solution was cooled to room temperature and filtered. The filtrate was washed with DMF, MeOH and CH_2Cl_2 and dried to obtain the title compound (608 mg, 0.65 mmol) in a yield of 98 %.

(6) Preparation of Wang resin-supported 2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid

Wang resin-supported 2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid methyl ester (570 ㎎, 0.47 mmol) obtained in step 5 was dissolved in THF, $LiOH \cdot H_2O$ (99 ㎎, 2.35 mmol) in MeOH-H_2O (2 : 1) was added thereto and the resulting mixture was refluxed for 5 hours. The resulting solution was cooled to room temperature and filtered. The filtrate was washed with MeOH and CH_2Cl_2, and dried to obtain the title compound (551 mg, 0.42 mmol) in a yield of 90 %.

Preparation Example 5: Preparation of Wang resin-supported 2-(2,4-difluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (R^1 = F, R^2 = H and R^3 = F)

(1) Preparation of 3-[(2,4-difluoro-benzimidoyl)-amino]-4-methoxy-benzoic acid methyl ester

Anhydrous *p*-toluene sulfonic acid (25.0 g, 137.43 mmol) was melted at 120 ℃ and 3-amino-4-methoxy benzoic acid methyl ester (10 g, 55.25 mmol) obtained in step 1 of Preparation Example 1 and 2,4-difluorobenzonitrile (11.53 g, 82.87 mol) were added thereto and stirred at 160 ℃ for 8 hours. The resulting solution was cooled to room temperature and the reaction was stopped by adding $NaHCO_3$ thereto. The resulting mixture was extracted with ethyl acetate, the extract was dried over $MgSO_4$ and concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography to obtain the title compound (10.0 g, 31.22 mmol) in a yield of 57%.

^{1}H NMR ($CDCl_3$): δ 8.31-8.22 (1H, m), 7.82-7.79 (1H, d), 7.65 (1H, s), 7.02-6.85 (3H, m), 3.88 (6H, s)

MW : 320

(2) Preparation of 2-(2,4-difluoro-phenyl)-7-methoxy-1H-benzoimidazole-4-carboxylic acid methyl ester

3-[(2,4-difluoro-benzimidoyl)-amino]-4-methoxy-benzoic acid

methyl ester (9.5 g, 29.66 mmol) obtained in step 1 was dissolved in 50% methanol and 5% NaOCl (53 ml, 35.71 mmol) was added dropwise thereto at room temperature. After 5 min, Na_2CO_3 (6.29 g, 59.34 mmol) was added dropwise thereto and refluxed for 5 min. The resulting solution was cooled to room temperature, extracted with ethyl acetate, and the extract was concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography to obtain the title compound (3.50 g, 11.0 mmol) in a yield of 37 %.

^{1}H NMR ($CDCl_3$): δ 10.99 (1H, bs). 8.65-8.57 (1H, m), .92 (1H, d), 7.10-6.97 (2H, m), 6.76 (1H, d), 4.13 (3H, s), 4.00 (3H, s)

MW : 318

(3) Preparation of 2-(2,4-difluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid

2-(2,4-difluoro-phenyl)-7-methoxy-1H-benzoimidazole-4-carboxylic acid methyl ester (2.24 g, 7.04 mmol) obtained in step 2 was dissolved in toluene, aluminum chloride (3.75 g, 28.12 mmol) was added thereto and refluxed for 8 hours. The resulting solution was cooled to room temperature, the reaction was stopped by adding 3 N HCl thereto and stirred for 30 min. The precipitate formed was filtered, washed with benzene and dried to obtain the title compound (1.70 g, 5.86 mmol) in a yield of 83%.

^{1}H NMR (CH_3OH-d_4): δ 8.13-8.03 (2H, m), 7.47-7.33 (2H, m), 7.04 (1H, d)

MW : 290

(4) Preparation of 2-(2,4-difluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid methyl ester

2-(2,4-difluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (1.70 mg, 5.86 mmol) obtained in step 3 was dissolved in methanol, $SOCl_2$ (8.2 ml, 112 mmol) was added dropwise thereto and refluxed for 15 hours. The resulting solution was cooled to room temperature, concentrated under a reduced pressure to remove methanol, and the residue was neutralized with $NaHCO_3$. Then, the neutralized residue was extracted

with ethyl acetate and concentrated under a reduced pressure to obtain a residue which was purified by silica gel chromatography to obtain the title compound (1.50 mg, 1.64 mmol) in a yield of 84 %.

^{1}H NMR (DMSO-d_6): δ 12.04 (1H, bs), .30-8.04 (1H, m), 7.73 (1H, d), 7.55-7.48 (1H, m), 7.33-7.27 (1H, m), 6.70 (1H, d), 4.01 (3H, s)
MW : 304

(5) Preparation of Wang resin-supported 2-(2,4-difluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid methyl ester

(4-bromomethylphenoxy)-methyl polystyrene Wang resin (476 mg, 0.67 mmol) was dissolved in DMF, and 2-(2,4-difluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid methyl ester (567 mg, 2.01 mmol) obtained in step 4, Cs_2CO_3 (655 mg, 2.01 mmol) and KI (334 mg, 2.01 mmol) were added thereto to be stirred at 50 to 60 ℃ for 12 hours. The resulting solution was cooled to room temperature and filtered. The filtrate was washed with DMF, MeOH and CH_2Cl_2 and dried to obtain the title compound (608 mg, 0.65 mmol) in a yield of 98 %.

(6) Preparation of Wang resin-supported 2-(2,4-difluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid

Wang resin-supported 2-(2,4-difluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid methyl ester (570 mg, 0.47 mmol) obtained in step 5 was dissolved in THF, $LiOH \cdot H_2O$ (99 mg, 2.35 mmol) in MeOH-H_2O was added thereto and the resulting mixture was refluxed for 5 hours. The resulting solution was cooled to room temperature and filtered. The filtrate was washed with MeOH and CH_2Cl_2, and dried to obtain the title compound (551 mg, 0.42 mmol) in a yield of 90 %.

Preparation Example 6: Preparation of Wang resin-supported 2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (R^1 = Cl, R^2 = H and R^3 = F)

(1) Preparation of 3-[(2-chloro-4-fluoro-benzimidoyl)-amino]-4-methoxy-benzoic acid methyl ester

Anhydrous *p*-toluene sulfonic acid (41.99 g, 220.76 mmol) was melted at 120 ℃ and 3-amino-4-methoxy benzoic acid methyl ester (20 g, 110.38 mmol) obtained in step 1 of Preparation Example 1 and 2-chloro-4-fluorobenzonitrile (25.76 g, 165.57 mol) were added thereto and stirred at 160 ℃ for 8 hours. The resulting solution was cooled to room temperature and the reaction was stopped by adding $NaHCO_3$ thereto. The resulting mixture was extracted with ethyl acetate, the extract was dried over $MgSO_4$ and concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography to obtain the title compound (26.70 g, 79.47 mmol) in a yield of 72%.

^{1}H NMR ($CDCl_3$): δ 7.92-7.75 (4H, m), 7.15-7.02 (3H, m), 3.87-3.81 (6H, d)
MW : 336

(2) Preparation of 2-(2-chloro-4-fluoro-phenyl)-7-methoxy-1H-benzoimidazole-4-carboxylic acid methyl ester

3-[(2-chloro-4-fluoro-benzimidoyl)-amino]-4-methoxy-benzoic acid methyl ester (10 g, 29.76 mmol) obtained in step 1 was dissolved in 50% methanol and 5% NaOCl (53 ml, 35.71 mmol) was added dropwise thereto at room temperature. After 5 min, Na_2CO_3 (6.31 g, 59.52 mmol) was added dropwise thereto and refluxed for 5 min. The resulting solution was cooled to room temperature, extracted with ethyl acetate, the extract was concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography to obtain the title compound (5.17 g, 15.48 mmol) in a yield of 52 %.

^{1}H NMR ($CDCl_3$): δ 8.18 (2H, t), .91 (1H, d), 7.30-7.25 (2H, t), 6.65 (1H, d), 6.85 (1H, d), 4.08 (3H, s), 3.98 (3H, s)
MW : 334

(3) Preparation of 2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid

2-(2-chloro-4-fluoro-phenyl)-7-methoxy-1H-benzoimidazole-4-

carboxylic acid methyl ester (3 g, 8.98 mmol) obtained in step 2 was dissolved in toluene and aluminum chloride (5.99 g, 44.90 mmol) was added thereto, refluxed for 8 hours. The resulting solution was cooled to room temperature, the reaction was stopped by adding 3 N HCl thereto and stirred for 30 min. The precipitate formed was filtered, washed with benzene and dried to obtain the title compound (1.87 g, 6.11 mmol) in a yield of 68%.

^{1}H NMR (CH_3OH-d_4): δ 8.19-8.15 (2H, t), 8.06 (1H, d), 7.50-7.44 (2H, t), 7.00 (1H, d)

MW : 306

(4) Preparation of 2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid methyl ester

2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (500 mg, 1.63 mmol) obtained in step 3 was dissolved in methanol, H_2SO_4 (0.43 ml, 8.15 mmol) was added dropwise thereto and refluxed for 15 hours. The resulting solution was cooled to room temperature, concentrated under a reduced pressure to remove methanol, and the residue was neutralized with $NaHCO_3$. Then, the neutralized residue was extracted with ethyl acetate and concentrated under a reduced pressure to obtain a residue which was purified by silica gel chromatography to obtain the title compound (393 mg, 1.23 mmol) in a yield of 67 %.

^{1}H NMR (CH_3OH-d_4): δ 8.22-8.18 (2H, t), 7.80 (1H, d), 7.32-7.26 (2H, t), 6.70 (1H, d), 3.97 (3H, s)

MW : 320

(5) Preparation of Wang resin-supported 2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid methyl ester

(4-bromomethylphenoxy)-methyl polystyrene Wang resin (476 mg, 0.67 mmol) was dissolved in DMF, and 2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid methyl ester (567 mg, 2.01 mmol) obtained in step 4, Cs_2CO_3 (655 mg, 2.01 mmol) and KI (334 mg, 2.01 mmol) were added thereto to be stirred at 50 to 60 ℃ for 12 hours. The resulting solution was cooled to room temperature and filtered. The

filtrate was washed with DMF, MeOH and CH_2Cl_2 and dried to obtain the title compound (608 mg, 0.65 mmol) in a yield of 98 %.

(6) Preparation of Wang resin-supported 2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid

Wang resin-supported 2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid methyl ester (570 mg, 0.47 mmol) obtained in step 5 was dissolved in THF, $LiOH \cdot H_2O$ (99 mg, 2.35 mmol) in MeOH-H_2O was added thereto and the resulting mixture was refluxed for 5 hours. The resulting solution was cooled to room temperature and filtered. The filtrate was washed with MeOH and CH_2Cl_2, and dried to obtain the title compound (551 mg, 0.42 mmol) in a yield of 90 %.

Preparation Example 7: Preparation of Wang resin-supported 2-(3-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (R^1 = H, R^2 = Cl and R^3 = F)

(1) Preparation of 3-[(3-chloro-4-fluoro-benzimidoyl)-amino]-4-methoxy-benzoic acid methyl ester

Anhydrous *p*-toluene sulfonic acid (10 g, 52.57 mmol) was melted at 120 ℃ and 3-amino-4-methoxy benzoic acid methyl ester (3.88 g, 21.44 mmol) obtained in step 1 of Preparation Example 1 and 3-chloro-4-fluorobenzonitrile (5.0 g, 32.14 mol) were added thereto and stirred at 160 ℃ for 8 hours. The resulting solution was cooled to room temperature and the reaction was stopped by adding $NaHCO_3$ thereto. The resulting mixture was extracted with ethyl acetate, the extract was dried over $MgSO_4$ and concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography to obtain the title compound (3.24 g, 9.62 mmol) in a yield of 45%.

^{1}H NMR ($CDCl_3$): δ 7.96-7.95 (1H, m), 7.76-7.73 (2H, m), 7.60 (1H, bs), 7.17-7.11 (1H, m), 6.93(1H, d), 3.85(3H, s), 3.84 (3H, d)

MW : 336

(2) Preparation of 2-(3-chloro-4-fluoro-phenyl)-7-methoxy-1H-benzoimidazole-4-carboxylic acid methyl ester

3-[(3-chloro-4-fluoro-benzimidoyl)-amino]-4-methoxy-benzoic acid methyl ester (3.24 g, 9.62 mmol) was dissolved in 50% methanol and 5% NaOCl (18 ml, 11.90 mmol) was added dropwise thereto at room temperature. After 5 min, Na_2CO_3 (2.04 g, 19.25 mmol) was added dropwise thereto and refluxed for 5 min. The resulting solution was cooled to room temperature, extracted with ethyl acetate, and the extract was concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography to obtain the title compound (0.95 g, 2.83 mmol) in a yield of 30 %.

^{1}H NMR ($CDCl_3$): δ 10.68 (1H, bs), 8.23-8.20 (1H, m), 7.96-7.91 (1H, m), 7.87 (1H, d), 7.27-7.20 (1H, m), 6.73 (1H, d), 4.10 (3H, s), 3.97 (3H, s)

MW : 334

(3) Preparation of 2-(3-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid

2-(3-chloro-4-fluoro-phenyl)-7-methoxy-1H-benzoimidazole-4-carboxylic acid methyl ester (0.95 g, 8.98 mmol) obtained in step 2 was dissolved in toluene, aluminum chloride (1.5 g, 11.25 mmol) was added thereto and refluxed for 8 hours. The resulting solution was cooled to room temperature, the reaction was stopped by adding 3 N HCl thereto and stirred for 30 min. The precipitate formed was filtered, washed with benzene and dried to obtain the title compound (0.81 g, 2.64 mmol) in a yield of 80%.

^{1}H NMR (MeOH-d_4): δ 8.34 (1H, dd), 8.22-8.08 (2H, m), 7.62 (1H, t), 7.03 (1H, d)

MW : 306

(4) Preparation of 2-(3-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid methyl ester

2-(3-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-

carboxylic acid (800 mg, 2.64 mmol) obtained in step 3 was dissolved in methanol, $SOCl_2$ (1.93 ml, 26.41 mmol) was added dropwise thereto and refluxed for 15 hours. The resulting solution was cooled to room temperature, concentrated under a reduced pressure to remove methanol, and the residue was neutralized with $NaHCO_3$. Then, the neutralized residue was extracted with ethyl acetate and concentrated under a reduced pressure to obtain a residue which was purified by silica gel chromatography to obtain the title compound (690 mg, 2.15 mmol) in a yield of 81 %.

^{1}H NMR (DMSO-d_6): δ 12.39 (1H, bs), 8.56 (1H, d), 8.30 (1H, bs), 7.72 (1H, d), 7.59 (1H, t), 6.69 (1H, d), 3.90 (3H, s)
MW : 320

(5) Preparation of Wang resin-supported 2-(3-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid methyl ester

(4-bromomethylphenoxy)-methyl polystyrene Wang resin (476 mg, 0.67 mmol) was dissolved in DMF, and 2-(3-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid methyl ester (567 mg, 2.01 mmol) obtained in step 4, Cs_2CO_3 (655 mg, 2.01 mmol) and KI (334 mg, 2.01 mmol) were added thereto to be stirred at 50 to 60 ℃ for 12 hours. The resulting solution was cooled to room temperature and filtered. The filtrate was washed with DMF, MeOH and CH_2Cl_2 and dried to obtain the title compound (608 mg, 0.65 mmol) in a yield of 98 %.

(6) Preparation of Wang resin-supported 2-(3-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid

Wang resin-supported 2-(3-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid methyl ester (570 mg, 0.47 mmol) obtained in step 5 was dissolved in THF, $LiOH{\cdot}H_2O$ (99 mg, 2.35 mmol) in MeOH-H_2O was added thereto and the resulting mixture was refluxed for 5 hours. The resulting solution was cooled to room temperature and filtered. The filtrate was washed with MeOH and CH_2Cl_2, and dried to obtain the title compound (551 mg, 0.42 mmol) in a yield of 90 %.

Example 1: Preparation of 7-hydroxy-2-phenyl-1H-benzoimidazole-4-

carboxylic acid amide ($R^4R^5NH_2 = NH_4Cl$)

Wang resin-supported 7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid (36 mg, 0.03 mmol) obtained in Preparation Example 1 was dissolved in 3 ml of DMF and aluminum chloride (5 mg, 0.09 mmol), EDCI (18 mg, 0.09 mmol), DMAP (11 mg, 0.09 mmol) and HOBt (12 mg, 0.09 mmol) were added thereto and the resulting mixture was stirred at room temperature. The resulting solution was filtered, the filtrate was washed with DMF, MeOH and CH_2Cl_2 and dried to obtain Wang resin-supported 7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid amide.

Then, 30 mg of Wang resin-supported 7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid amide was dissolved in 0.2 ml of CH_2Cl_2, 0.2 ml of trifluoroacetic acid was added thereto and stirred for 30 min. The resulting solution was filtered, the filtrate was washed with MeOH and CH_2Cl_2 and dried to obtain the title compound in a yield of 90%.

^{1}H NMR (CH_3OH-d_4): δ 8.15 (2H, d), 7.84 (1H, d), 7.78-7.56 (3H, m), 6.83 (1H, m)

MW : 253

Example 2 to 203

The same procedure as described in Example 1 was repeated using $R^4R^5NH_2$ listed in Table 2 to obtain the compounds 2 to 203, respectively.

Table 2

Com No.	Pre No.	Chemical compound	$R^4N(CH_2)_nR^5$	n	^1H NMR (CH_3OH-d_4)	MW
2	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid-phenylamide	aniline	0	δ 8.10 (2H, d), 7.87 (1H, d), 7.85-7.60 (3H, m), 7`.40 (2H, d), 07.39-7.28 (2H, m), 7.27-7.20 (1H, m), 6.89 (1H, d)	329
3	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid(4-hydroxy-phenyl)-amide	4-hydroxyaniline	0	δ 8.28-8.03 (3H, m), 7.98-7.82 (1H, d), 7.79-7.56 (3H, m), 7.48 (2H, d), 6.85-6.72 (2H, m)	345
4	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid (4-amino-phenyl)-amide	1,4-diaminophenylene	0	δ 8.28-8.14 (2H, m), 8.03-7.91 (3H, m), 7.71-7.56 (3H, m), 7.46-7.34 (2H, d), 6.89-6.76 (1H, d)	344
5	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid(4-hydroxy-cyclohexyl)-amide	4-hydroxycyclohexylamine	0	δ 8.08 (2H, d), 7.82 (1H, d), 7.78-7.50 (3H, m), 6.88 (1H, d), 4.15-3.82 (1H, m), 3.70-3.54 (1H, m), 2.30-1.90 (4H, m), 1.85-1.20 (4H, m)	351
6	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid(4-hydroxymethyl-phenyl)-amide	4-(hydroxymethyl)aniline	0	δ 8.20 (2H, d), 7.92 (2H, d), 7.81-7.70 (1H, m), 7.69-7.58 (3H, m), 7.50-7.30 (1H, m), 7.29-7.10 (1H, m), 6.89 (1H, d), 4.65 (2H, s)	359

7	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid[4-(2-hydroxy-ethyl)-phenyl]-amide	4-(hydroxyethyl)aniline	0	δ 8.14 (2H, d), 7.98 (1H, d), 7.78-7.60 (5H, m), 7.30-7.18 (2H, m), 6.88 (1H, d), 4.65 (1H, t), 3.73 (1H, t), 3.02 (1H, t), 2.81 (1H, t)	373
8	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid[4-(2-amino-ethyl)-phenyl]-amide	4-(aminoethyl) aniline	0	δ 8.27-8.16 (2H, m), 7.95 (1H, d), 7.78 (2H, d), 7.66-7.54 (3H, m), 7.44 (2H, d), 6.86 (1H, d), 3.19 (2H, t), 2.92 (2H, t)	372
9	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid{4-[2-(toluene-4-sulfonyl amino)-ethyl]-phenyl}-amide	*N*-[2-(4-amino-phenyl)-ethyl]-4-methylbenzenesulfonamide	0	δ 8.20-8.02 (3H, m), 8.00 (2H, d), 7.70-7.68 (5H, m), 7.38 (2H, d), 7.16 (2H, d), 6.94 (1H, d), 3.10 (2H, t), 2.73 (2H, t), 2.43 (3H, s)	526
10	1	7-hydroxy-2-phenyl-1H-bezoimidazole-4-carboxylic acid[4-(2-methanesulfonylamino-ethyl)-phenyl]-amide	*N*-[2-(4-amino-phenyl)-ethyl]-4-methane sulfonamide	0	δ 8.13 (2H, d), 7.98 (1H, d), 7.75-7.53 (5H, m), 7.29 (2H, d), 6.91 (1H, d), 3.30 (2H, t), 2.82 (2H, t)	450

11	1	7-hydroxy-2-phenyl-1H-bezoimidazole-4-carboxylic acid {4-[2-(1,3-dioxo-1,3-dihydro-isoindole-2-yl)-ethyl]-phenyl}-amide	2-[2-(4-amino phenyl)-ethyl]-isoindole-1,3-dione	0	δ 7.45 (2H, d), 6.98-6.84 (4H, m), 6.82 (2H, d), 6.73-6.54 (4H, m), 6.30 (2H, d), 5.89 (1H, d), 2.91 (2H, t), 2.00 (2H, t)	502
12	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid{4-[2-(thiophene-2-sulfonylamino)-ethyl]-phenyl}-amide	thiophene-2-sulfonic acid [2-(4-amino-phenyl)-ethyl]-amide	0	δ 8.15 (2H, d), 8.06 (1H, d), 7.80-7.55 (7H, m), 7.23-7.10 (3H, m), 7.05 (1H, d), 3.16 (2H, t), 2.80 (2H, t)	518
13	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid[4-(2-ethanesulfonylamino-ethyl)-phenyl]-amide	*N*-[2-(4-amino-phenyl)-ethyl]-ethanesulfonamide	0	δ 8.17 (2H, d), 8.03 (1H, d), 7.77-7.68 (5H, m), 7.27 (2H, d), 7.01 (1H, d), 3.31 (2H, t), 2.99 (2H, q), 2.85 (2H, t), 1.23 (3H, t)	464
14	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid phenylamide	aniline	0	δ 8.18 (2H, d), 8.11 (1H, d), 7.80 (2H, d), 7.67 (2H, d), 7.40 (2H, t), 7.15 (1H, t), 6.89 (1H, d)	363

15	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (4-hydroy-cyclohexyl)-amide	4-hydroxycyclohexylamine	0	δ 8.15 (2H, d), 7.84 (1H, d), 7.69 (2H, d), 6.90 (1H, d), 3.95 (1H, m), 3.58 (1H, m), 2.28-1.95 (4H, m), 1.83-1.25 (4H, m)	385
16	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {4-[2-(toluene-4-sulfonylamino)-ethyl]-phenyl}-amide	*N*-[2-(4-amino-phenyl)-ethyl]-4-methyl-benzensulfonamide	0	δ 8.18 (2H, d), 7.98 (1H, d), 7.80-7.60 (6H, m), 7.36 (2H, d), 7.16 (2H, d), 6.94 (1H, d), 3.09 (2H, t), 2.74 (2H, t), 2.41 (3H, s)	560
17	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [4-(2-methanesulfonylamino-ethyl)-phenyl]-amide	*N*-[2-(4-amino-phenyl)-ethyl]-methenesulfonylamide	0	δ 8.15 (1H, d), 7.94 (1H, d), 7.72 (2H, d), 7.62 (2H, d), 7.28 (2H, d), 6.85 (1H, d), 3.32 (2H, t), 2.85 (3H,s), 2.84 (2H, t)	484
18	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {4-[2-(1,3-dioxo-1,3-dihydro-isoindole-2-yl)-ethyl]-phenyl}-amide	2-[2-(4-amino-phenyl)-ethyl]-isoindole-1,3-dione	0	δ 8.16 (2H, d), 8.02 (1H, d), 7.86-7.76 (4H, m), 7.75-7.61 (4H, m), 7.22 (2H, d), 6.95 (1H, m), 3.90 (2H, t), 2.97 (2H, t)	536

19	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {4-[2-(thiophene-2-sulfonylamino-ethyl)-phenyl]-amide	thiophene-2-sulfonic acid[2-(4-amino-phenyl)-ethyl]-amide	0	δ 8.15 (2H, d), 7.97 (2H, d), 7.75-7.57 (6H, m), 7.19 (2H, d), 6.92 (1H, d), 3.17 (2H, t), 2.77 (2H, t)	552
20	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [4-(2-ethanesulfonylamino-ethyl)-phenyl]-amide	*N*-[2-(4-amino-phenyl)-ethyl]-ethanasulfonylamide	0	δ 8.17 (2H, d), 8.09 (2H, d), 7.73 (2H, d), 7.63 (2H, d), 7.29 (2H, d), 3.31 (2H, t), 2.98 (2H, q), 2.85 (2H, t), 1.24 (3H, t)	498
21	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid amide	ammonium chloride	0	δ 7.98-7.70 (2H, m), 7.69-7.52 (1H, m), 7.28-7.00 (1H, m), 6.95-6.82 (1H, m)	321
22	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid phenylamide	aniline	0	δ 8.02 (1H, d), 8.01-7.82 (1H, m), 7.81-7.65 (3H, m), 7.64-7.45 (1H, m), 7.43-7.20 (2H, t), 7.42-7.02 (1H, t), 6.90 (1H, d)	397
23	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (4-hydroxy-cyclohexyl)-amide	4-hydroxy-cyclohexylamine	0	δ 8.02-7.68 (2H, m), 7.68-7.48 (1H, m), 7.20-7.03 (1H, m), 6.88 (1H, d), 3.93 (1H, m), 3.58 (1H, m), 2.25-1.85 (4H, m), 1.84-1.39 (4H, m)	419

24	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [4-(2-amino-ethyl)-phenyl]-amide	4-aminophenethylamine	0	δ 7.97 (2H, d), 7.85-7.63 (3H, m), 7.56 (1H, d), 7.38-7.20 (2H, m), 6.82 (1H, d), 3.18 (2H, t), 2.96 (2H, t)	440
25	3	2-(2,4-Dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (4-amino-phenyl)-amide	1,4-phenylene diamine	0	δ 8.06-7.81 (4H, m), 7.80-7.64 (1H, s), 7.58 (1H, d), 7.38 (2H, d), 6.84 (1H, d)	412
26	3	2-(2,4-Dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (4-hydroxy methyl-phenyl)-amide	4-aminobenzy alcohol	0	δ 8.00 (1H, d), 7.98-7.84 (1H, m), 7.75 (1H, m), 7.74-7.52 (2H, m), 7.50-7.26 (1H, m), 7.25-7.05 (2H, m), 7.04-6.80 (1H, m)	427
27	3	2-(2,4-Dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [4-(2-hyroxy-ethyl)-phenyl]-amide	4-aminophenethyl alcohol	0	δ 8.15-7.86 (2H, m), 7.85-7.45 (3H, m), 7.25 (2H, d), 7.20-6.75 (2H, m), 4.58 (1H, t), 3.75 (1H, t), 3.05 (1H, t), 2.81 (1H, t)	441

28	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {4-[2-(toluene-4-sulfonylamino)-ethyl]-phenyl}-amide	*N*-[2-(4-amino-phenyl)-ethyl]-4-methyl-benzensulfonamide	0	δ 8.20-8.02 (3H, m), 8.00 (2H, d), 7.70-7.68 (3H, m), 7.38 (2H, d), 7.16 (2H, d), 6.94 (1H, d), 3.10 (2H, t), 2.73 (2H, t), 2.43 (3H, s)	594
29	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [4-(2-methanesulfonylamino-ethyl)-phenyl]-amide	*N*-[2-(4-amino-phenyl)-ethyl]-methanesulfonamide	0	δ 8.02 (1H, d), 8.01-7.78 (1H, m), 7.70 (2H, d), 7.67-7.50 (1H, m), 7.25 (2H, d), 6.90 (2H, d), 3.28 (2H, t), 2.84 (2H, t), 2.82 (3H,s)	518
30	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {4-[2-(1,3-dioxo-1,3-dihydro-isoindole-2-yl)-ethyl]-phenyl}-amide	2-[2-(4-amino-phenyl)-ethyl]-isoindole-1,3-dione	0	δ 7.10 (1H, d), 6.99-6.81 (6H, m), 6.80-6.65 (3H, m), 6.28 (2H, d), 5.92 (1H, d), 2.88 (2H, t), 1.97 (2H, t)	570
31	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {4-[2-(thiophene-2-sulfonylamino)-ethyl]-phenyl}-amide	thiophene-2-sulfonic acid[2-(4-amino-phenyl)-ethyl]-amide	0	δ 8.08 (1H, d), 7.88 (2H, m), 7.83 (1H, d), 7.75 (1H, d), 7.68-7.65 (3H, m), 7.63 (1H, d), 7.17-7.01 (2H, m), 6.97 (1H, d), 3.16 (2H, t), 2.77 (2H, t)	586

32	3	2-(2,4-dichloro-phenyl)-7-hydrioxy-1H-benzoimidazole-4-carboxylic acid [4-(2-ethanesulfonylamino-ethyl)-phenyl]-amide	*N*-[2-(4-amino-phenyl)-ethyl]-ethanesulfonamide	0	δ 8.11 (1H, d), 7.95-7.82 (2H, m), 7.75-7.60 (3H, m), 7.28 (2H, d), 7.01 (1H, d), 3.31 (2H, t), 2.98 (2H, q), 2.85 (2H, t), 1.24 (3H, t)	532
33	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [4-(2-methane sulfonylamino-ethyl)-phenyl]-amide	*N*-[2-(4-amino-phenyl)-ethyl]-methanesulfonamide	0	δ 8.23-8.15 (2H, m), 7.91 (1H, d), 7.69 (2H, d), 7.39 (2H, t), 7.26 (2H, d), 6.83 (1H, d), 3.31 (2H, t), 2.85-2.78 (5H, m)	
34	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {4-[2-(toluene-4-sulfonylamino)-ethyl]-phenyl}-amide	*N*-[2-(4-amino-phenyl)-ethyl]-4-methyl-benzensulfonamide	0	δ 8.25-8.21 (2H, m), 7.98-7.93 (2H, m), 7.71-7.64 (4H, m), 7.41-7.34 (3H, m), 7.14 (2H, d), 6.87 (1H, d), 3.08 (2H, t), 2.73 (2H, t), 2.40 (3H, s)	
35	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [4-(2-methanesulfonylamino-ethyl)-phenyl]-amide	*N*-[2-(4-amino-phenyl)-ethyl]-ethanesulfonamide	0	δ 8.05 (2H, t), 7.78 (1H, d), 7.30 (2H, t), 7.14 (2H, d), 6.77 (2H, d), 6.69 (1H, d), 3.78 (2H, q), 3.35 (2H, t), 2.90 (2H, t), 1.28 (3H, t)	

36	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (4-morpholin-4-yl-phenyl)-amide	4-morpholin-4-yl-phenylamine	0		
37	5	2-(2,4-difluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [4-(2-methanesulfonylamino-ethyl)-phenyl]-amide	*N*-[2-(4-amino-phenyl)-ethyl]-methanesulfonamide	0	δ 7.90 (1H, d), 7.62 (1H, d), 7.31-7.17 (4H, m), 6.81 (1H, d), 3.22 (2H, t), 2.76 (5H,m)	
38	5	2-(2,4-difluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {4-[2-(toluene-4-sulfonylamino)-ethyl]-phenyl}amide	*N*-[2-(4-amino-phenyl)-ethyl]-4-methyl-benzensulfonamide	0	δ 7.99 (1H, m), 7.74 (1H, d), 7.50 (2H, d), 7.33-7.26 (2H, m), 7.23 (4H, m), 6.94 (2H, d), 6.81 (1H, d), 3.58 (2H, t), 2.82 (2H, t), 2.23 (3H, s)	
39	5	2-(2,4-difluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [4-(2-methanesulfonylamino-ethyl)-phenyl]-amide	*N*-[2-(4-amino-phenyl)-ethyl]-ethanesulfonamide	0	δ 8.19-8.00 (2H, m), 7.70 (1H, d), 7.43-7.26 (4H, m), 6.87 (1H, d), 3.98 (2H, t), 2.97 (2H, q), 2.86 (2H, t), 1.25 (3H, t)	

40	6	2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {4-[2-(toluene-4-sulfonylamino)-ethyl]-phenyl}amide	*N*-[2-(4-amino-phenyl)-ethyl]-4-methyl-benzensulfonamide)	0	δ 8.01-7.93 (1H, m), 7.65 (3H, t), 7.53-7.44 (2H, m), 7.33 (4H, m), 7.11 (2H, d), 6.80 (1H, d), 3.09 (2H, t), 2.72 (2H, t), 2.38 (3H, s)	
41	6	2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [4-(2-methanesulfonylamino-ethyl)-phenyl]-amide	*N*-[2-(4-amino-phenyl)-ethyl]-methanesulfonamide	0	δ 8.06 (1H, m), 7.97 (1H, d), 7.68-7.61 (3H, m), 7.40 (1H, m), 7.27 (2H, m), 6.97 (1H, m), 3.61 (2H, t), 2.84 (5H, m)	
42	6	2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [4-(2-methanesulfonylamino-ethyl)-phenyl]-amide	*N*-[2-(4-amino-phenyl)-ethyl]ethanesulfonamide	0	δ 8.07 (1H, m), 7.97 (1H, d), 7.68-7.40 (3H, m), 7.28-7.18 (3H, m), 6.99 (1H, d), 3.61 (2H, t), 2.96 (2H, q), 2.84 (2H, t), 1.28 (3H, t)	

43	7	2-(3-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {4-[2-(toluene-4-sulfonylamino)-ethyl]-phenyl}amide	*N*-[2-(4-amino-phenyl)-ethyl]-4-methyl-benzensulfonamide	0	δ 8.18 (1H, d), 7.90 (1H, m), 7.72 (1H, d), 7.47 (2H, d), 7.39 (1H, m), 7.13-7.06 (4H, m), 6.95(2H, d), 6.75 (1H, d), 3.63 (2H, t), 2.85 (2H, t), 2.23 (3H, s)	
44	7	2-(3-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [4-(2-methanesulfonylamino-ethyl)-phenyl]-amide	*N*-[2-(4-amino-phenyl)-ethyl]-ethanesulfonamide	0	δ 8.27 (1H, d), 8.10 (1H, m), 7.85 (1H, d), 7.64 (2H, d), 7.41 (1H, t), 7.22 (2H, d), 6.76 (1H, d), 3.26 (2H, t), 2.94 (2H, q), 2.80 (2H, t), 1.22(3H, t)	
45	7	2-(3-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [4-(2-methanesulfonylamino-ethyl)-phenyl]-amide	*N*-[2-(4-amino-phenyl)-ethyl]-methanesulfonamide	0	δ 8.31 (1H, d), 8.12 (1H, m), 7.91 (1H, d), 7.68 (2H, d), 7.47 (1H, t), 7.26 (2H, d), 6.83 (1H, d), 3.31 (2H, t), 2.85 (5H, m)	
46	1	cyclohexyl-(7-hydroxy-2-phenyl-1H-benzoimidazole-4-yl)-methanone	piperidine	0	δ 7.31-7.23 (5H, m), 7.05 (1H, d), 6.64 (1H, d), 3.53-3.29 (4H, m), 1.82-1.41 (6H, m)	320
47	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid cyclohexyl-amide	piperidine	0	δ 8.10 (2H, d), 7.88 (1H, d), 7.66 (2H, d), 6.92 (1H, d), 3.53-3.29 (4H, m), 1.82-1.41 (6H, m)	355

48	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-yl-piperidine-1-yl-methanone	piperidine	0	δ 7.31-7.23 (3H, m), 7.05 (1H, d), 6.64 (1H, d), 3.53-3.29 (4H, m), 1.82-1.41 (6H, m)	389
49	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid(4-nitro-benzyl)-amide	4-nitrobenzylamine-hydrochloride)	1	δ 8.20 (2H, d), 8.13 (2H, d), 7.82 (1H, d), 7.82-7.55 (5H, m), 6.87 (1H, d), 4.75 (2H, s)	388
50	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid (4-amino-benzyl)-amide	4-aminobenzylamine-dihydrochloride	1	δ 8.15 (2H, d), 7.82 (1H, d), 7.72-7.52 (5H, m), 7.33 (2H, d), 6.87 (1H, d), 4.70 (2H, s)	358
51	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid benzylamide	benzylamine	1	δ 8.10 (2H, d), 7.87 (1H, d), 7.85-7.60 (3H, m), 7.40 (2H, d), 7.39-7.28 (2H, m), 7.27-7.20 (1H, m), 6.89 (1H, d), 4.66 (2H, s)	343
52	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid benzylamide	benzylamine	1	δ 8.10 (2H, d), 7.88 (1H, d), 7.66 (2H, d), 7.42-7.23 (5H, m), 6.92 (1H, d), 4.68 (2H, s)	377
53	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid(4-nitro-benzyl)-amide	4-nitrobenzylamine-hydrochloride	1	δ 8.20 (2H, d), 7.90 (2H, d), 7.88 (1H, s), 7.69-7.51 (4H, m), 6.91 (1H, d), 4.76 (2H, s)	422

54	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (4-amino-benzyl)-amide	4-aminobenzylamine-hydroxychloride	1	δ 8.20 (2H, d), 7.90 (2H, d), 7.88 (1H, s), 7.69-7.51 (4H, m), 6.91 (1H, d), 4.76 (2H, s)	392
55	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid benzylamide	benzylamine	1	δ 8.10 (2H, d), 7.88 (1H, d), 7.66 (2H, d), 7.37-7.23 (4H, m), 6.92 (1H, d), 4.68 (2H, s)	411
56	3	2-(2,4-Dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (4-nitro-benzyl)-amide	4-nitrobenzylamine	1	δ 8.20 (2H, d), 7.90 (2H, t), 7.88 (1H, s), 7.69-7.51 (3H, m), 6.91 (1H, d), 4.76 (2H, s)	456
57	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid -phenethyl-amide	phenethylamine	2	δ 8.10 (2H, d), 7.78 (1H, d), 7.77-7.58 (3H, m), 7.44-7.18 (5H, m), 6.85 (1H, s), 3.68 (2H, t), 2.98 (2H, t)	357
58	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid (4-hydroxy-pheneethyl)-amide	4-hydroxyphenethylamine	2	δ 8.02-7.92 (2H, m), 7.77 (1H, d), 7.62-7.42 (3H, m), 7.11 (2H, d) , 6.78 (1H, d), 6.70 (2H, d), 3.72 (2H, t), 2.83 (2H, t)	373
59	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid (4-nitro-phenethyl)-amide	4-nitrophenethylamine	2	δ 8.10 (2H, d), 8.01 (2H, d), 7.75 (1H, d), 7.69-7.52 (3H, m), 7.50 (2H, d), 6.85 (1H, d), 3.75 (2H, t), 3.08 (2H, t)	402

60	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid (4-amino-phenethyl)-amino	4-aminophenethylamine	2	δ 8.11 (2H, d), 7.78 (1H, d), 7.74-7.59 (3H, m), 7.46 (2H, d), 7.31 (2H, d), 6.85 (1H, d), 3.72 (2H, t), 3.02 (2H, t)	372
61	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid (2-amino-ethyl)-amide	ethylenediamine	2	δ 7.95-7.70 (2H, m), 7.69 (1H, d), 7.60-7.42 (1H, m), 7.41-7.23 (2H, m), 3.77 (2H, t), 3.25 (2H, t)	296
62	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid (4-hydroxy-3-methoxy-phenethyl)-amide	4-hydroxy-3-methoxyphenethylamine	2	δ 8.10-8.00 (2H, m), 7.78 (1H, d), 7.69-7.52 (3H, m), 6.91-6.77 (2H, m), 6.72 (2H, d), 3.73 (3H, s), 3.70 (2H, t), 2.89 (2H, t)	403
63	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid (3-hydroxy-4-methoxy-phenethyl)-amide	3-hydroxy-4-methoxyphenethylamine	2	δ 8.08-7.93 (2H, m), 7.78 (1H, d), 7.62-7.50 (2H, m), 6.98-6.52 (5H, m), 3.80 (3H, s), 3.68 (2H, t), 2.82 (2H, t)	403
64	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid[2-(4-methanesulfonylamino-phenyl)-ethyl]-amide	*N*-[4-(2-amino-ethyl)-phenyl]-methanesulfonamide	2	δ 8.07 (1H, d), 7.77 (1H, d), 7.65-7.61 (4H, m), 7.28 (2H, d), 7.18 (2H, d), 6.85 (1H, d), 3.71 (2H, t), 2.95 (2H, t), 2.85 (3H, s)	450

65	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid{2-[4-(toluene-4-sulfonyl amino)-phenyl]-ethyl}-amide	*N*-[4-(2-amino-ethyl)-phenyl]-4-methyl-benzensulfonamide	2	δ 8.09 (2H, d), 7.76-7.54 (5H, m), 7.33-7.30 (3H, m), 7.20-7.13 (2H, m), 7.01-6.87 (3H, m), 3.73 (1H, t), 3.63 (1H, t), 3.01 (1H, t), 2.88 (1H, t), 2.44 (3H, s)	526
66	1	7-hydroxy-2-phenyl-H-benzoimidazole-4-carboxylic acid (2-morpholin-4-yl-ethyl)-amide	4-(2-aminoethyl) morpholine	2	δ 8.17-8.12 (2H, m), 7.88 (1H, d), 7.77-7.71 (3H, m), 7.00-6.95 (1H, m), 4.02-3.75 (4H, m), 3.89 (2H, t), 3.47 (2H, t), 3.46-3.00 (4H, t)	366
67	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid{2-[4-(1,3-dioxo-1,3-dihydro-isoindole-2-yl)-phenyl]-ethyl}-amide	2-[4-(2-amino-ethyl)-phenyl]-isoindole-1,3-dione	2	δ 8.14 (2H, d), 7.97-7.68 (8H, m), 7.40 (4H, dd), 6.93 (1H, d), 3.74 (2H, t), 3.05 (2H, t)	502
68	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid [2-(4-ethanesulfonylamino-phenyl)-ethyl]-amide	*N*-[4-(2-amino-ethyl)-phenyl]-ethansulfonamide	2	δ 8.15 (2H, d), 7.79-7.72 (4H, m), 7.22 (4H, dd), 6.97 (1H, d), 3.66 (2H, t), 2.99 (2H, q), 2.89 (2H, t), 1.22 (3H, t)	

69	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid (5-mitropyridine-2-amino-ethyl)-amide	2-(2-aminoethylamino)-5-nitropyridine	2	δ 8.84 (1H, d), 8.13-8.05 (3H, m), 7.80-7.65 (4H, m), 6.90 (1H, d), 6.57 (1H, d), 3.71-3.60 (4H, m)	418
70	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid (2-pyridine-2-yl-ethyl)-amide	2-(2-aminoethyl)-pyridine	2	8.71 (1H, d), 8.44 (1H, t), 8.13-7.99 (4H, m), 7.85 (1H, t), 7.76-7.70 (2H, m), 6.99 (1H, d), 6.83 (1H, d), 3.97 (2H, t), 3.42 (2H, t)	358
71	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid phenethyl amide	phenethylamine	2	δ 8.03 (2H, d), 7.79 (1H, d), 7.64 (2H, m), 7.37-7.15 (5H, m), 6.84 (1H, d), 3.75 (2H, t), 2.99 (2H, t)	391
72	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (4-nitro-phenethyl)-amide	4-nitrophenethylamine	2	δ 8.18 (2H, d), 8.05 (2H, d), 7.80 (1H, d), 7.64 (2H, d), 7.56 (2H, d), 6.88 (1H, d), 3.80 (2H, t), 3.11 (2H, t)	436
73	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (4-amino-phenethyl)-amide	4-aminophenethylamine	2	δ 8.11 (2H, d), 7.83 (1H, d), 7.64 (2H, d), 7.50 (2H, d), 7.31 (2H, d), 6.82 (1H, d), 3.78 (2H, t), 3.07 (2H, t)	406

74	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (4-hydroxy-phenethyl)-amide	4-hydroxyphenethylamine	2	δ7.82 (1H, d), 7.73 (2H, d), 7.65 (2H, d), 7.12 (2H, d), 7.00 (1H, d), 6.86 (1H, d), 6.74 (1H, d), 3.71 (2H, t), 2.87 (2H, t)	407
75	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-methane sulfonylamino-phenyl)-ethyl]-amide	*N*-[4-(2-amino-ethyl-phenyl)-methanesulfonamide	2	δ 8.08 (2H, d), 7.79 (1H, d), 7.69 (2H, d), 7.29-7.16 (4H, dd), 6.89 (1H, d), 3.71 (2H, t), 2.95 (2H, t), 2.88 (3H, s)	484
76	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {2-[4-(toluene-4-sulfonylamino)-phenyl]-ethyl}-amine	*N*-[4-(2-amino-ethyl)-phenyl]-4-methyl-benzenesulfonamide	2	δ 8.08 (2H, d), 7.77 (1H, d), 7.69 (2H, d), 7.55 (1H, d), 7.15 (3H, m), 6.98 (2H, d), 6.88 (1H, d), 3.65 (2H, t), 2.86 (2H, t), 2.31 (3H, s)	560
77	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (3-hydroxy-4-methoxy-phenethyl)-amide	3-hydroxy-4-methoxy-phenethylamine	2	δ 8.10-7.37 (3H, m), 7.36-6.43 (6H, m), 3.72 (3H, s), 3.70 (2H, t), 2.81 (2H, t)	437

78	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (2-morpholin-4-yl-ethyl)-amide	4-(2-aminoethyl)morpholine	2	δ 8.16 (2H, d), 7.88 (1H, d), 7.70 (2H, d), 6.94 (1H, d), 4.14-3.92 (2H, m), 3.90 (2H, t), 3.89-3.72 (2H, m), 3.84-3.57 (2H, m), 3.48 (2H, t), 3.30-3.04 (2H, m)	400
79	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid -2-[4-(1,3-dioxo-1,3-dihydro-isoindole-2-yl)-phenyl]-ethyl-amide	2-[4-(2-amino-ethyl)-phenyl]-isoindole-1,3-dione	2	δ 8.10 (2H, d), 7.91-7.85 (4H, m), 7.80 (1H, d), 7.68 (2H, m), 6.98 (1H, d), 7.40 (4H, dd), 6.93 (1H, m), 3.75 (2H, t), 3.07 (2H, t)	536
80	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-ethane sulfonylamino-phenyl)-ethyl]-amide	*N*-[4-(2-amino-ethyl)-phenyl]-ethanesulfonamide	2	δ 8.13-8.05 (3H, m), 7.80-7.65 (3H, m), 7.28-7.16 (4H, m), 3.69 (2H, t), 2.99 (2H, q), 2.89 (2H, t), 1.28 (3H, t)	498
81	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (5-nitropyridine-2-amino-ethyl)-amide	2-(2-aminoethylamino)-5-nitropyridine	2	δ 8.83 (1H, d), 8.11-8.05 (1H, m), 7.86-7.81 (3H, m), 7.68-7.60 (2H, m), 6.90 (1H, d), 6.60-6.54 (1H, d), 3.71-3.60 (4H, m)	452

82	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (2-pyridine-2-yl-ethyl)-amide	2-(2-aminoethyl)-pyridine	2	δ 8.70 (1H, d), 8.43 (1H, t), 8.13-8.09 (3H, m), 8.01 (1H, d), 7.94 (1H, d), 7.77 (1H, d), 7.61 (2H, d), 4.01 (2H, t), 3.42 (2H, t)	392
83	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(1H-imidazol-4-yl)-ethyl]amide	histamine	2	δ 8.81(s, 1H), 8.12(d, 2H), 7.80(d, 1H), 7.65(d, 2H), 7.40(s, 1H), 6.83(d, 1H), 3.84(t, 2H), 3.12(t, 2H)	
84	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-hydroxy-phenyl)-ethyl]-amide	4-hydroxyphenethylamine	2	δ 8.05(d, 2H), 7.79(d, 1H), 7.65(d, 2H), 7.12(d, 2H), 6.85(d, 1H), 6.72(d, 2H), 3.70(t, 2H), 2.87(t, 2H)	
85	2	2-(4-Chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(5-acetylamino-pyridin-2-ylamino)-ethyl]-amide	4-acetyl-2-pyridylethylamine	2	δ 8.57(s, 1H), 8.20~8.00(m, 3H), 8.02(br, 1H), 7.75~7.60(m, 3H), 7.38(d, 1H), 6.88(d, 1H), 4.12(t, 2H), 3.68(t, 2H), 2.12(s, 3H)	

86	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (2-{4-[2-(4-methyl-piperazin-1-yl)-acetylamino]-phenyl}-ethyl)-amide	*N*-[4-(2-amino-ethyl)-phenyl]-2-(4-methyl-piperazin-1-yl)-acetamide	2	δ 8.03(m, 2H), 7.80(d, 1H), 7.60(d, 2H), 7.57(d, 2H), 7.29(d, 2H), 6.83(d, 1H), 3.75(t, 2H), 3.34(s, 2H), 3.10~2.75(m, 13H)	
87	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (2-{4-[2-(4-ethyl-piperazin-1-yl)-acetylamino]-phenyl}-ethyl)-amide	*N*-[4-(2-amino-ethyl)-phenyl]-2-(4-ethyl-piperazin-1-yl)-acetamide	2	δ 8.03(m, 2H), 7.79(d, 1H), 7.61(d, 2H), 7.53(d, 2H), 7.29(d, 2H), 6.84(d, 1H), 3.75(t, 2H), 3.34(s, 2H), 3.25(q, 2H), 3.05~2.75(m, 8H), 1.35(t, 3H	
88	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {2-[4-(2-dimethylamino-acetylamino)-phenyl]-ethyl}-amide	*N*-[4-(2-amino-ethyl)-phenyl]-2-dimethylamino-acetamide	2	δ 8.03(d, 2H), 7.80(d, 1H), 7.60(d, 2H), 7.54(t, 2H), 7.32(d, 2H), 6.81(d, 1H), 4.08(s, 2H), 3.76(t, 2H), 2.95(m, 8H)	

89	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {2-[4-(2-diethylamino-acetylamino)-phenyl]-ethyl}-amide	*N*-[4-(2-amino-ethyl)-phenyl]-2-diethylamino-acetamide	2	δ 8.02(d, 2H), 7.80(d, 1H), 7.60(d, 2H), 7.54(d, 2H), 7.32(d, 2H), 6.81(d, 1H), 4.06(s, 2H), 3.77(t, 2H), 3.32(q, 4H), 2.99(t, 2H), 1.35(t, 6H)	
90	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-amino-phenyl)-ethyl]-amide	4-aminophenethylamine	2	δ 8.13(d, 2H), 7.78(d, 1H), 7.62(d, 2H), 7.51(d, 2H), 7.29(d, 2H), 6.77(d, 1H), 3.79(t, 2H), 3.69(t, 2H	
91	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(5-amino-pyridin-2-ylamino)-ethyl]-amide	*N*-(2-amino-ethyl)-pyridine-2,5-diamine	2	δ 8.73(s, 1H), 8.22(d, 1H), 8.09(d, 1H), 7.88(m, 2H), 7.60(d, 1H), 7.47(d, 1H), 7.13(d, 1H), 6.78(m, 1H), 3.87(t, 2H), 3.75(t, 2H)	
92	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {2-[4-(2-morpholin-4-yl-acetylamino)-phenyl]-ethyl}-amide	*N*-[4-(2-amino-ethyl)-phenyl]-2-morpholin-4-yl-acetamide	2	δ 8.03(d, 2H), 7.80(d, 1H), 7.60(d, 2H), 7.54(d, 2H), 7.31(d, 2H), 6.81(d, 1H), 3.12(s, 2H), 3.98(br, 4H), 3.77(t, 2H), 3.44(br, 4H), 2.98(t, 2H)	

93	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-dimethylamino-phenyl)-ethyl]-amide	*N,N*-(dimethylamino)phenethylamine	2	δ 8.13(d, 2H), 7.78(d, 1H), 7.62(d, 2H), 7.51(d, 2H), 7.29(d, 1H), 6.77(d, 1H), 3.81(t, 2H), 3.15(s, 6H), 3.08(t, 2H)	
94	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {2-[4-(2-morpholin-4-yl-ethoxy)phenyl]-ethyl}-amide	2-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-ethylamine	2	δ 8.06(d, 2H), 7.79(d, 1H), 7.73(d, 2H), 7.28(d, 2H), 6.94(d, 2H), 6.83(d, 1H), 4.31(m, 2H), 3.99(br, 2H), 3.95~3.65(m, 4H), 3.65~3.50(m, 4H), 3.32(m, 2H), 2.95(m, 2H)	
95	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (2-{4-[2-(4-methyl-piperazin-1-yl)ethoxy]-phenyl}-ethyl)-amide	2-{4-[2-(4-methyl-piperazin-1-yl)-ethoxy]-phenyl}-ethylamine	2	δ 8.17(d, 2H), 7.78(d, 1H), 7.40(t, 2H), 7.23(d, 2H), 6.90(m, 3H), 4.25(t, 2H), 3.67(t, 2H), 3.50~3.30(m, 10H), 2.90(m, 5H)	
96	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(2-hydroxy-phenyl)-ethyl]-amide	2-hydroxyphenethylamine	2	δ 8.05(d, 2H), 7.79(d, 1H), 7.62(d, 2H), 7.18(d, 1H), 07.05(d, 1H), 6.90~6.70(m, 3H), 3.70(t, 2H), 3.02(t, 2H)	

97	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(2-methoxy-phenyl)-ethyl]-amide	2-methoxyphenethylamine	2	δ 8.00(d, 2H), 7.81(d, 1H), 7.57(d, 2H), 7.24(d, 1H), 6.95(m, 1H), 6.85(m, 1H), 6.73(d, 2H), 3.76(s, 3H), 3.64(t, 2H), 2.98(t, 2H)	
98	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(3-bromo-phenyl)-ethyl]-amide	3-bromophenethylamine	2	δ 8.00(d, 2H), 7.79(d, 1H), 7.02~7.50(m, 3H), 7.40~7.20(m, 3H), 6.74(d, 1H), 3.81(t, 2H), 3.01(t, 2H)	
99	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid phenethyl-amide	phenethylamine	2	δ 7.92-7.66 (3H, m), 7.65-7.38 (1H, m), 7.37-7.00 (5H, m), 7.44-7.18 (5H, m), 6.85 (1H, d), 3.68 (2H, t), 2.98 (2H, t)	425
100	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid(4-amino-phenethyl)-amide	4-nitrophenethylamine	2	δ 8.08 (2H, d), 7.90-7.31 (5H, m), 7.20-6.97 (1H, m), 6.82 (1H, d), 3.76 (2H, t), 3.09 (2H, t)	470
101	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (4-hydroxy-3-methoxy-phenethyl)-amide	4-hydroxy-3-methoxyphenethylamine	2	δ 7.95-7.68 (3H, m), 7.67-7.40 (2H, m), 7.20-6.92 (1H, m), 6.82 (2H, t), 6.68 (1H, d), 3.72 (2H, t), 3.60 (3H, s), 2.88 (2H, t)	471

102	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (3-hydroxy-4-methoxy-phenethyl)-amide	3-hydroxy-4-methoxyphenethylamine	2	δ 8.10-7.37 (3H, m), 7.36-6.43 (6H, m), 3.72 (3H, s), 3.70 (2H, t), 2.81 (2H, t)	471
103	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (2-amino-ethyl)-amide	ethylenediamine	2	δ 8.10 (2H, d), 7.88 (1H, d), 7.66 (2H, d), 7.37-7.23 (4H, m), 6.92 (1H, d), 3.77 (2H, t), 3.25 (2H, t)	364
104	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (4-hydroxy phenethyl)-amide	4-hydroxyphenethylamine	2	δ 7.94-7.64 (3H, m), 7.62-7.39 (1H, m), 7.28-6.97 (3H, m), 6.96-6.78 (1H, m), 6.68 (1H, d), 3.64 (2H, t), 2.82 (2H, t)	441
105	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {2-[4-(toluene-4-sulfonylamino)-phenyl]-ethyl}-amide	*N*-[4-(2-amino-ethyl)-phemphenyl]-4-methyl-benzensulfonamide	2	δ 7.95-7.70 (2H, m), 7.69-7.43 (3H, m), 7.42-7.23 (3H, m), 7.22-7.03 (2H, m), 7.01 (1H, d), 6.98-6.77 (2H, m), 3.81-3.52 (2H, m), 3.10-2.73 (2H, m), 3.01 (1H, t), 2.88 (1H, t), 2.48 (3H, s)	594

106	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-methanesulfonylamino-phenyl)-ethyl]-amide	*N*-[4-(2-amino-ethyl)-phenyl]-methanesulfonamide	2	δ 7.92-7.78 (3H, m), 7.68 (1H, d), 7.24 (4H, dd), 6.96 (1H, d), 3.68 (2H, t), 2.93 (2H, t), 2.90 (3H, s)	518
107	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {2-[4-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-phenyl]-ethyl}-amide	2-[4-(2-amino-ethyl)-phenyl]-isoindole-1,3-dione	2	δ 7.92-7.83 (7H, m), 7.67 (1H, d), 7.38 (4H, dd), 6.98 (1H, d), 3.72 (2H, t), 3.05 (2H, t)	570
108	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (2- morpholin-4-yl-ethyl)-amide	4-(2-aminoethyl) morpholine	2	δ 8.02-7.80 (3H, m), 7.65 (1H, d), 6.98 (1H, d), 4.14-3.92 (2H, m), 3.88 (2H, t), 3.89-3.72 (2H, m), 3.84-3.57 (2H, m), 3.44 (2H, t), 3.30-3.04 (2H, m)	434
109	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-ethanesulfonylamino-phenyl)-ethyl]-amide	*N*-[4-(2-amino-ethyl)-phenyl]-ethanesulfonamide	2	δ 7.91-7.75 (3H, m), 7.68 (1H, d), 7.21 (4H, dd), 6.99 (1H, d), 3.66 (2H, t), 2.99 (2H, q), 2.89 (2H, t), 1.28 (3H, t)	532

110	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (5- nitropyridine-2-amino-ethyl)-amide	2-(2-aminoethylamino)-5-nitropyridine	2	δ 8.83 (1H, d), 8.11-8.05 (1H, m), 7.86-7.81 (3H, m), 7.68-7.60 (1H, m), 6.90 (1H, d), 6.60-6.54 (1H, d), 3.71-3.60 (4H, m)	486
111	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (2-pyridin-2-yl-ethyl)-amide	2-(2-aminoethyl)-pyridine	2	δ 8.70 (1H, d), 8.40 (1H, t), 8.07-7.50 (6H, m), 6.83 (1H, d), 3.95 (2H, t), 3.38 (2H, t)	426
112	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-acetyl amino-phenyl)-ethyl]-amide	4-(acetylamino)phenethylamine	2	δ 7.85~7.78(m, 3H), 7.61(d, 1H), 7.25(d, 2H), 7.15(d, 2H), 6.86(d, 1H), 3.69(t, 2H), 2.95(t, 2H), 2.88(s, 3H)	
113	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-pentanoyl amino-phenyl)ethyl]-amide	4-(pentanoylamino)phenethylamine	2	δ 7.90~7.80(m, 3H), 7.72(d, 1H), 7.61(d, 2H), 7.20(d, 2H), 6.89(d, 1H), 3.68(t, 2H), 2.89(t, 2H), 2.35(t, 2H), 1.65(m, 2H), 1.38(m, 2H), 0.96(t, 3H)	

114	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-methanesulfonylamino-phenyl)-ethyl]-amide	*N*-[4-(2-amino-ethyl)-phenyl]-methanesulfonamide	2	δ 8.15-8.10 (2H, m), 7.78 (1H, d), 7.46 (2H, t), 7.27 (2H, d), 7.18 (2H, d), 6.87 (1H, d), 3.70 (2H, t), 2.97 (2H, t), 2.87 (3H, s)	
115	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {2-[4-(toluene-4-sulfonylamino)-phenyl]-ethyl}-amide	*N*-[4-(2-amino-ethyl)-phenyl]-p-toluenesulfonamide	2		
116	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-ethanesulfonylamino-phenyl)-ethyl]-amide	*N*-[4-(2-amino-ethyl)-phenyl]-ethanesulfonamide	2	δ 8.17 (2H, m), 7.77 (1H, d), 7.44 (2H, t), 7.25 (2H, d), 7.17 (2H, d), 6.92 (1H, d), 3.67 (2H, t), 3.02 (2H, q), 2.96 (2H, t), 1.26 (3H, t)	
117	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-acetylamino-phenyl)-ethyl]-amide	*N*-[4-(2-amino-ethyl)-phenyl]-acetamide	2	δ 8.1~8.2 (m, 2H), 7.58 (d,1H), 7.44 (m, 4H), 7.34 (m, 2H), 6.92 (d, 1H), 3.66 (t, 2H), 2.90 (t, 2H), 2.09 (s, 1H)	

118	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-methyl-piperazin-1-yl)-ethyl]-amide	2-(4-methyl-piperazin-1-yl)-ethylamine	2	δ 8.25~8.16(m, 2H), 8.05(d, 1H), 7.48~7.37(m, 2H), 6.88(d, 1H), 3.70~3.50(m, 10H), 3.14(t, 2H), 2.96(s, 3H), 2.12(t, 2H)	
119	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (2-morpholin-4-yl-ethyl)-amide	2-morpholin-4-yl-ethylamine	2	δ 8.22(m, 2H), 7.85(d, 1H), 7.41(t, 2H), 6.90(d, 1H), 4.20~3.60(m, 8H), 3.48(t, 2H), 3.34~3.10(br, 2H)	
120	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-pentanoyl amino-phenyl)-ethyl]-amide	pentanoic acid [4-(2-amino-ethyl)-phenyl]-amide	2	δ 8.08(m, 2H), 7.74(d, 1H), 7.45(d, 2H), 7.35(t, 2H), 7.18(d, 2H), 6.86(d, 1H), 3.66(t, 2H), 2.86(t, 2H), 2.33(t, 2H), 1.64(m, 2H), 1.39(m, 2H), 0.93(t, 3H)	
121	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-hydroxy-phenyl)-ethyl]-amide	4-hydroxyphenethylamine	2	δ 8.14(m, 2H), 7.78(d, 1H), 7.44(t, 2H), 7.09(d, 2H), 6.89(d, 1H), 6.72(d, 2H), 3.66(t, 2H), 2.86(t, 2H)	

122	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(5-nitro-pyridin-2-ylamino)-ethyl]-amide	*N*-(5-nitro-pyridin-2-yl)-ethane-1,2-diamine	2	δ 8.84(s, 1H), 8.21~8.17(m, 3H), 7.79(d, 1H), 7.44(t, 2H), 6.92(d, 1H), 6.63(br, 1H), 3.90~3.60(m, 4H)	
123	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(5-methanesulfonylamino-pyridin-2-ylamino)-ethyl]-amide	*N*-[6-(2-Amino-ethylamino)-pyridin-3-yl]-methanesulfonamide	2	δ 8.24~8.19(m, 2H), 7.95~7.75(m, 3H), 7.43(t, 2H), 7.15(d, 1H), 6.92(d, 1H), 3.80~3.65(m, 4H), 2.99(t, 3H)	
124	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {2-[5-(toluene-4-sulfonylamino)-pyridin-2-ylamino]-ethyl}-amide	*N*-[6-(2-amino-ethylamino)-pyridin-3-yl]-p-toluenesulfonamide	2	δ 8.23(m, 2H), 7.81(d, 1H), 7.52(m, 4H), 7.40~7.20(m, 4H), 7.01(d, 1H), 6.82(d, 1H), 3.75(t, 2H), 3.66(t, 2H), 2.36(s, 3H)	
125	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(1H-imidazol-4-yl)-ethyl]-amide	histamine	2	δ 8.81(s, 1H), 8.19(m, 2H), 7.80(d, 1H), 7.50~7.30(m, 3H), 6.90(d, 1H), 3.80(t, 2H), 3.11(t, 2H)	

126	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(5-acetylamino-pyridin-2-yl-amino)-ethyl]-amide	*N*-[6-(2-amino-ethylamino)-pyridin-3-yl]-acetamide	2	δ 8.58(s, 1H), 8.22(m, 2H), 8.04(br, 1H), 7.69(d, 1H), 7.50~7.35(m, 3H), 6.90(d, 1H), 4.11(t, 2H), 3.69(t, 2H), 2.11(s, 3H)	
127	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (2-{4-[2-(4-methyl-piperazin-1-yl)-acetylamino]-phenyl}-ethyl)-amide	*N*-[4-(2-amino-ethyl)-phenyl]-2-(4-methyl-piperazin-1-yl)-acetamide	2	δ 8.10~7.80(m, 2H), 7.69(d, 1H), 7.43(d, 2H), 7.25(t, 2H), 7.19(d, 2H), 6.76(d, 1H), 3.63(t, 2H), 3.21(s, 2H), 2.90~2.78(m, 13H)	
128	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (2-{4-[2-(4-ethyl-piperazin-1-yl)-acetylamino]-phenyl}-ethyl)-amide	*N*-[4-(2-amino-ethyl)-phenyl]-2-(4-ethyl-piperazin-1-yl)-acetamide	2	δ 8.13(m, 2H), 7.79(d, 1H), 7.52(d, 2H), 7.37(t, 2H), 7.27(d, 2H), 6.85(d, 1H), 3.72(t, 2H), 3.30(s, 2H), 3.24(q, 2H), 3.05~2.85(m, 10H), 1.35(t, 3H)	
129	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {2-[4-(2-dimethylamino-acetylamino)-phenyl]-ethyl}-amide	*N*-[4-(2-amino-ethyl)-phenyl]-2-dimethylamino-acetamide	2	δ 8.11(m, 2H), 7.78(d, 1H), 7.53(d, 2H), 7.40~7.25(m, 4H), 6.83(d, 1H), 4.09(s, 2H), 3.74(t, 2H), 2.94(m, 8H)	

130	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {2-[4-(2-diethylamino-acetylamino)-phenyl]-ethyl}-amide	*N*-[4-(2-amino-ethyl)-phenyl]-2-diethylamino-acetamide	2	δ 8.13(m, 2H), 7.79(d, 1H), 7.54(d, 2H), 7.39(t, 2H), 7.30(d, 2H), 6.86(d, 1H), 4.08(s, 2H), 3.72(t, 2H), 3.33(q, 4H), 2.96(t, 2H), 1.35(t, 6H)	
131	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-amino-phenyl)-ethyl]-amide	4-aminophenethylamine	2	δ 8.20(m, 2H), 7.79(d, 1H), 7.49(d, 2H), 7.42(t, 2H), 7.32(d, 2H), 6.86(d, 1H), 3.74(t, 2H), 3.06(t, 2H)	
132	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-morpholin-4-yl-phenyl)-ethyl]-amide	2-(4-morpholin-4-yl-phenyl)-ethylamine	2	δ 8.14(m, 2H), 7.78(d, 1H), 7.41(d, 2H), 7.35(d, 1H), 7.14(d, 2H), 6.85(d, 1H), 3.89(m, 4H), 3.71(t, 2H), 3.28(m, 4H), 2.96(t, 2H)	
133	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {2-[4-(3-diethylamino-pyrrolidin-1-yl)-phenyl]-ethyl}-amide	{1-[4-(2-amino-ethyl)-phenyl]-pyrrolidin-3-yl}-diethyl-amine	2	δ 8.13 (m, 1H), 7.78 (d, 1H), 7.32~7.20 (m, 4H), 7.11 (s, 1H), 6.74 (m, 2H), 6.48 (d, 1H), 3.60 (t, 2H), 2.90 (t, 2H), 2.82~2.71 (m, 6H), 2.40 (q, 4H), 1.65 (m, 1H), 1.02 (t, 6H)	

134	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {2-[4-(2-morpholin-4-yl-acetylamino)-phenyl]-ethyl}-amide	*N*-[4-(2-amino-ethyl)-phenyl]-2-morpholin-4-yl-acetamide	2	δ 8.15(m, 2H), 7.79(d, 1H), 7.53(d, 2H), 7.39(t, 2H), 7.29(d, 2H), 6.87(d, 1H), 4.13(s, 2H), 3.97(br, 4H), 3.72(q, 2H), 3.44(br, 4H), 2.97(t, 2H)	
135	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-dimethylamino-phenyl)-ethyl]-amide	*N,N*-(dimethylamino)phenethylamine	2	δ 8.20(m, 3H), 7.78(d, 1H), 7.54(m, 3H), 7.43(t, 2H), 6.84(d, 1H), 3.75(t, 2H), 3.21(s, 6H), 3.07(t, 2H)	
136	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {2-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-ethyl}-amide	2-[4-(2-morpholin-4-yl-ethoxy)-phenyl]-ethylamine	2	δ 8.18(m, 2H), 7.79(d, 1H), 7.42(t, 2H), 7.26(d, 2H), 7.00~6.85(m, 3H), 4.33(m, 2H), 4.10~4.00(br, 2H), 3.95~3.75(br, 2H), 3.75~3.50(m, 8H), 3.32(m, 4H), 2.95(m, 2H)	
137	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(2-hydroxy-phenyl)-ethyl]-amide	2-hydroxyphenethylamine	2	δ 8.18(m, 2H), 7.78(d, 1H), 7.38(t, 2H), 7.14(d, 1H), 7.03(d, 1H), 6.88~6.74(m, 3H), 3.77(t, 2H), 2.98(t, 2H)	

138	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(2-methoxy-phenyl)-ethyl]-amide	2-methoxyphenethylamine	2	δ 8.18~8.05(m, 2H), 7.78(d, 1H), 7.45~7.25(m, 3H), 7.20(m, 2H), 6.95(d, 1H), 6.82(d, 1H), 3.78(s, 3H), 3.73(t, 2H), 2.99(t, 2H)	
139	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(3-bromo-phenyl)-ethyl]-amide	3-bromophenethylamine	2	δ 8.12(m, 2H), 7.80(d, 1H), 7.49(s, 1H), 7.38~7.18(m, 5H), 6.83(d, 1H), 3.76(t, 2H), 2.97(t, 2H)	
140	5	2-(2,4-difluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-methanesulfonylamino-phenyl)-ethyl]-amide	*N*-[4-(2-amino-ethyl)-phenyl]-methanesulfonamide	2	δ 7.92-7.89 (1H, m), 7.74 (1H, m), 7.30-7.11 (6H, m), 6.74 (1H, d), 3.67 (2H, bs), 2.89 (2H, bs), 2.82 (3H, s)	
141	5	2-(2,4-difluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {2-[4-(toluene-4-sulfonylamino)-phenyl]-ethyl}amide	*N*-[4-(2-amino-ethyl)-phenyl]-p-toluenesulfonamide	2	δ 7.99 (1H, m), 7.74 (1H, d), 7.50 (2H, d), 7.33-7.26 (2H, m), 7.23 (4H, m), 6.94 (2H, d), 6.81 (1H, d), 3.58 (2H, t), 2.82 (2H, t), 2.23 (3H, s)	

142	5	2-(2,4-difluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-ethanesulfonylamino-phenyl)-ethyl]-amide	*N*-[4-(2-amino-ethyl)-phenyl]-ethanesulfonamide	2	δ 8.06 (1H, d), 7.81 (1H, d), 7.51-7.15 (6H, m), 6.88 (1H, d), 3.67 (2H, t), 3.01 (2H, q), 2.92 (2H, t), 1.25 (3H, m)	
143	6	2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-methanesulfonylamino-phenyl)-ethyl]-amide	*N*-[4-(2-amino-ethyl)-phenyl]-methanesulfonamide	2	δ 7.94 (1H, m), 7.84 (1H, m), 7.62 (1H, m), 7.43 (2H, m), 7.38-7.24 (3H, m), 6.95 (1H, d), 3.65 (2H, t), 2.99-2.83 (5H, m)	
144	6	2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {2-[4-(toluene-4-sulfonylamino)-phenyl]-ethyl}amide	*N*-[4-(2-amino-ethyl)-phenyl]-p-toluenesulfonamide	2	δ 7.91 (1H, m), 7.81 (1H, d), 7.62-7.54 (3H, m), 7.42 (1H, m), 7.20-7.11 (4H, m), 7.05-6.93 (3H, m), 3.61 (2H, t), 2.86 (2H, t), 2.32 (3H, s)	
145	6	2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-ethanesulfonylamino-phenyl)-ethyl]-amide	*N*-[4-(2-amino-ethyl)-phenyl]-ethanesulfonamide	2	δ 7.83 (2H, m), 7.56 (1H, m), 7.36 (1H, m), 7.18-7.11 (4H, m), 7.38-7.24 (3H, m), 6.92 (1H, d), 3.60 (2H, t), 2.99 (4H, m), 1.23 (3H, s)	

146	6	2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-acetylamino-phenyl)-ethyl]-amide	*N*-[4-(2-amino-ethyl)-phenyl]-acetamide	2	δ 8.00~7.91(m, 2H), 7.57(d, 1H), 7.48~7.34(m, 3H), 7.19(d, 2H), 6.92(d, 1H), 3.66(t, 2H), 2.9(t, 2H), 2.09(s, 3H)	
147	6	2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (2-morpholin-4-yl-ethyl)-amide	2-morpholin-4-yl-ethylamine	2	δ 8.00~7.90(m, 2H), 7.60(d, 1H), 7.43(t, 1H), 6.95(d, 1H), 4.20~3.60(m, 8H), 3.46(t, 2H), 3.34~3.10(br, 2H)	
148	6	2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-methyl-piperazin-1-yl)-ethyl]-amide	2-(4-methyl-piperazin-1-yl)-ethylamine	2	δ 7.98(m, 2H), 7.59(d, 1H), 7.40(t, 1H), 6.93(d, 1H), 3.80~3.50(br, 10H), 3.21(t, 2H), 2.95(s, 3H), 2.06(t, 2H)	
149	6	2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-pentanoylamino-phenyl)-ethyl]-amide	pentanoic acid [4-(2-amino-ethyl)-phenyl]-amide	2	δ 7.92~7.82(m, 2H), 7.57(d, 1H), 7.46~7.37(m, 3H), 7.20(d, 2H), 6.92(d, 1H), 3.66(t, 2H), 2.91(t, 2H), 2.34(t, 2H), 1.66(m, 2H), 1.40(m, 2H), 0.95(t, 3H)	

150	6	2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-hydroxy-phenyl)-ethyl]-amide	4-hydroxyphenethylamine	2	δ 7.92~7.83(m, 2H), 7.62(d, 1H), 7.43(t, 1H), 7.07(d, 2H), 6.94(d, 1H), 6.69(d, 2H), 3.62(t, 2H), 2.85(t, 2H)	
151	6	2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(5-nitro-pyridin-2-ylamino)-ethyl]-amide	*N*-(5-nitro-pyridin-2-yl)-ethane-1,2-diamine	2	δ 8.85(s, 1H), 8.12(br, 1H), 7.79~7.85(m, 3H), 7.63(d, 1H), 7.42(t, 1H), 6.95(d, 1H), 6.62(br, 1H), 3.90~3.60(m, 4H)	
152	6	2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(5-methanesulfonylamino-pyridin-2-ylamino)-ethyl]-amide	*N*-[6-(2-amino-ethylamino)-pyridin-3-yl]-methanesulfonamide	2	δ 8.05~7.85(m, 3H), 7.79(d, 1H), 7.61(d, 1H), 7.42(t, 1H), 7.14(d, 1H), 6.94(d, 1H), 3.80~3.60(m, 4H), 2.92(t, 3H)	
153	6	2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {2-[5-(toluene-4-sulfonylamino)-pyridin-2-ylamino]-ethyl}-amide	*N*-[6-(2-amino-ethylamino)-pyridin-3-yl]-p-toluenesulfonamide	2	δ 7.92(m, 1H), 7.89(d, 1H), 7.58(d, 2H), 7.45(m, 3H), 7.29(m, 3H), 6.92(d, 1H), 6.78(d, 1H), 3.72(t, 2H), 3.61(t, 2H), 2.37(s, 3H)	

154	6	2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(1H-imidazol-4-yl)-ethyl]-amide	histamine	2	δ 8.79(s, 1H), 8.00~7.0 2H), 7.62(d, 1H), 7.50~7.35(m, 2H), 6.93(d, 1H), 3.76(t, 2H), 3.76(t, 2H), 3.10(t, 2H)	
155	6	2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(5-acetylamino-pyridin-2-ylamino)-ethyl]-amide	*N*-[6-(2-amino-ethylamino)-pyridin-3-yl]-acetamide	2	δ 8.57(s, 1H), 8.10~7.95(m, 2H), 7.88(d, 1H), 7.74(d, 1H), 7.50~7.30(m, 2H), 6.95(d, 1H), 4.10(t, 2H), 3.65(t, 2H), 2.13(s, 3H)	
156	6	2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (2-{4-[2-(4-methyl-piperazin-1-yl)-acetylamino]-phenyl}-ethyl)-amide	*N*-[4-(2-Amino-ethyl)-phenyl]-2-(4-methyl-piperazin-1-yl)-acetamide	2	δ 7.97~7.80(m, 2H), 7.61(d, 1H), 7.59(d, 2H), 7.40(t, 1H), 7.25(d, 2H), 6.92(d, 1H), 3.67(t, 2H), 3.34(s, 2H), 3.10~2.75(m, 13H)	

157	6	2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (2-{4-[2-(4-ethyl-piperazin-1-yl)-acetylamino]-phenyl}-ethyl)-amide	*N*-[4-(2-amino-ethyl)-phenyl]-2-(4-ethyl-piperazin-1-yl)-acetamide	2	δ 7.97~7.83(m, 2H), 7.61(d, 1H), 7.50(d, 2H), 7.39(t, 1H), 7.25(d, 2H), 6.91(d, 1H), 3.67(t, 2H), 3.34(s, 4H), 3.21(q, 2H), 3.05~2.75(m, 8H), 1.35(t, 3H)	
158	6	2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {2-[4-(2-dimethylamino-acetylamino)-phenyl]-ethyl}-amide	*N*-[4-(2-amino-ethyl)-phenyl]-2-dimethylamino-acetamide	2	δ 7.99(m, 1H), 7.84~7.70(m, 2H), 7.52(d, 2H), 7.35~7.25(m, 3H), 6.77(d, 1H), 4.08(s, 2H), 3.73(s, 2H), 2.97(m, 8H)	
159	6	2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {2-[4-(2-diethylamino-acetylamino)-phenyl]-ethyl}-amide	*N*-[4-(2-amino-ethyl)-phenyl]-2-diethylamino-acetamide	2	δ 7.94~7.82(m, 2H), 7.60(d, 1H), 7.52(d, 2H), 7.40(t, 1H), 7.28(d, 2H), 6.89(d, 1H), 4.08(s, 2H), 3.68(t, 2H), 3.31(q, 4H), 2.94(t, 2H), 1.34(t, 6H)	
160	7	2-(3-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid {2-[4-(toluene-4-sulfonylamino)-phenyl]-ethyl}amide	*N*-[4-(2-amino-ethyl)-phenyl]-p-toluenesulfonamide	2	(1H, d), 7.90 (1H, m), 7.72 (1H, d), 7.47 (2H, d), 7.39 (1H, m), 7.13-7.06 (4H, m), 6.95(2H, d), 6.75 (1H, d), 3.63 (2H, t), 2.85 (2H, t), 2.23 (3H, s)	

161	7	2-(3-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [2-(4-methanesulfonylamino-phenyl)-ethyl]-amide	*N*-[4-(2-amino-ethyl)-phenyl]-methanesulfonamide	2	δ 8.19 (1H, d), 7.95 (1H, m), 7.74 (1H, d), 7.42 (1H, t), 7.24 (2H, d), 7.13 (2H, d), 6.75 (1H, d), 3.68 (2H, t), 2.91 (2H, t), 2.81 (3H, s)	
162	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid butylamide	n-butylamine	3	δ 7.95-7.70 (2H, m), 7.69 (1H, d), 7.60-7.42 (1H, m), 7.41-7.23 (2H, m), 3.42 (2H, t), 1.78-1.56 (2H, m), 1.55-1.34 (2H, t), 0.97 (3H, t)	309
163	1	7-Hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid (3-amino-propyl)-amide	1,3-diaminopropane	3 3	δ 8.10 (1H, d), 7.90 (1H, d), 7.68 (1H, d), 7.67-7.53 (3H, m), 6.81 (1H, d), 3.65 (2H, t), 3.22-3.00 (2H, t), 2.05 (2H, t)	310
164	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid [3-(2-oxo-prolidine-1-yl)-propyl]-amide	1-(3-aminopropyl)-2-prolidinone	3	δ 8.04 (1H, d), 7.81 (1H, d), 7.75-7.66 (3H, m), 6.96 (1H, d), 6.87 (1H, d), 3.53-3.41 (6H, m), 2.39 (2H, t), 2.03 (2H, t), 1.90 (2H, m)	378
165	1	7-hydroxy -2- phenyl-1H-benzoimidazole-4-carboxylic acid (3-imidazol-1-yl-propyl)-amide	1-(3-aminopropyl)imidazole	3	δ 9.05 (1H, s), 8.17 (2H, d), 7.84 (1H, d), 7.75 (1H, s), 7.72-7.62 (3H, m), 7.55 (1H, s), 6.88 (1H, d), 4.40 (2H, t), 3.57 (2H, t), 2.28 (2H, m)	361

166	1	7-hydroxy-2- phenyl-1H-benzoimidazole-4-carboxylic acid (3-morphorine-4-yl-propyl)-amide	4-(3-aminopropyl)morphorine	3	δ 8.20-8.11 (2H, m), 7.86 (2H, d), 7.84-7.69 (1H, m), 7.63-7.59 (2H, m), 4.10 (2H, t), 4.06 (2H, t), 3.80 (2H, t), 3.65 (2H, t), 3.54 (2H, t), 3.15 (2H, t), 2.14 (2H, m)	380
167	1	7-hydroxy-2-phenyl-1H-benzoimidazole-4-carboxylic acid [3-(2-methyl-imidazol-1-yl)-propyl]-amide	3-(2-methyl-imidazol-1-yl)-propylamine	3	δ 8.18-8.11 (2H, m), 7.84 (1H, d), 7.73-7.63 (4H, m), 7.40 (1H, d), 6.89 (1H, d), 4.28 (2H, t), 3.59 (2H, t), 2.63 (3H, s), 2.25 (2H, m)	
168	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid butylamide	n-butylamine	3	δ 8.10 (2H, d), 7.88 (1H, d), 7.66 (2H, d), 6.92 (1H, d), 3.42 (2H, t), 1.78-1.56 (2H, m), 1.55-1.34 (2H, t), 0.97 (3H, t)	343
169	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [3-(2-oxo-prolidin-1-yl)-propyl]-amide	1-(3-aminopropyl)-2-pyrrolidone	3	δ 8.21-8.11 (2H, m), 7.82 (1H, d), 7.63-7.53 (2H, m), 6.86 (1H, m), 3.60-3.38 (6H, m), 2.38 (2H, t), 2.03 (2H, t), 1.89 (2H, m)	412
170	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (3-imidazole-1-yl-propyl)-amide	1-(3-aminopropyl)imidazole	3	δ 9.03 (1H, d), 8.18 (2H, t), 7.81 (1H, d), 7.74 (1H, d), 7.64-7.53 (3H, m), 6.84 (1H, d), 4.40 (2H, t), 3.60 (2H, t), 2.29 (2H, m)	395

171	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (3-morphorine-4-yl-propyl)-amide	4-(3-aminopropyl)-morphorine	3	δ 8.21-8.10 (2H, m), 7.85 (1H, d), 7.61-7.54 (2H, m), 6.80 (1H, d), 4.05 (2H, t), 3.81 (2H, t), 3.68-3.46 (4H, m), 3.17 (2H, t), 2.11 (2H, m)	414
172	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [3-(2-pentyl-imidazol-1-yl)-propyl]-amide	3-(2-phenyl-imidazol-1-yl)-propylamine	3	δ 8.13 (2H, d), 7.87 (1H, d), 7.70 (1H, d), 7.64-7.53 (5H, m), 7.47-7.25 (3H, m), 6.80 (1H, d), 4.41 (2H, t), 3.53 (1H, t), 2.27 (2H, m)	473
173	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [3-(4-methyl-imidazol-1-yl)-propyl]-amide	3-(4-methyl-imidazole-1-yl)-propylamine	3	δ 8.85 (1H, d), 8.17 (2H, t), 7.87 (1H, m), 7.68-7.57 (2H, m), 7.40 (1H, d), 6.89 (1H, d), 4.32 (2H, t), 3.59 (2H, m), 2.37-2.20 (5H, m)	409
174	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [3-(4,5-dichloro-imidazol-1-yl)-propyl]-amide	3-(4,5-dichloro-imidazoel-1-yl)-propylamine	3	δ 8.13 (2H, t), 7.85-7.78 (2H, m), 7.65-7.55 (2H, m), 6.87 (1H, d), 4.18 (2H, t), 3.54 (2H, m), 2.18 (2H, m)	474
175	2	2-(4-chloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [3-(2-methyl-imidazol-1-yl)-propyl]-amide	3-(2-methyl-imidazole-1-yl)-propylamine	3	δ 8.21-8.09 (3H, m), 7.68 (1H, d), 7.60-7.55 (3H, m), 7.36 (1H, d), 4.28 (2H, t), 3.63 (2H, m), 2.60 (3H, s), 2.28 (2H, m)	421

176	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid butylamide	n-butylamine	3	δ 8.10 (2H, d), 7.88 (1H, d), 7.66 (2H, d), 7.37-7.23 (4H, m), 6.92 (1H, d), 3.42 (2H, t), 1.78-1.56 (2H, m), 1.55-1.34 (2H, t), 0.97 (3H, t)	377
177	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [3-(2-oxo-pyrolidin-1-yl)-propyl]-amide	1-(3-aminopropyl)-2-pyrolidione	3	δ 8.07-7.74 (3H, m), 7.73-7.49 (1H, m), 6.90 (1H, d), 3.60-3.38 (6H, m), 2.38 (2H, t), 2.03 (2H, t), 1.89 (2H, m)	446
178	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (3-imidazol-1-yl-propyl)-amide	1-(3-aminopropyl)imidazole	3	δ 9.02 (1H, s), 7.90-7.72 (4H, m), 7.64-7.46 (2H, m), 6.88 (1H, d), 4.37 (2H, t), 3.53 (2H, t), 2.26 (2H, m)	429
179	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (3-morphorin-4-yl-propyl)-amide	4-(3-aminopropyl)morphorine	3	δ 8.03-7.76 (3H, m), 7.75-7.45 (1H, m), 6.85 (1H, d), 4.05 (2H, t), 3.81 (2H, t), 3.68-3.46 (4H, m), 3.17 (2H, t), 2.11 (2H, m)	448
180	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [3-(2-phenyl-imidazol-1-yl)-propyl]-amide	3-(2-phenyl-imidazol-1-yl)-propylamine	3	δ 8.15 (d, 2H), 8.11 (s, 1H), 7.86 (s, 1H), 7.64~7.29 (m, 5H), 7.29~7.25 (m, 3H), 6.56 (d, 1H), 4.41 (t, 2H), 3.53 (t, 2H), 2.27 (q, 3H)	

181	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [3-(4-methyl-imidazol-1-yl)-propyl]-amide	3-(4-methyl-imidazol-1-yl)-propylamine	3	δ 8.84 (s, 1H), 7.91~7.73 (m, 3H), 7.58 (m, 1H), 7.38 (s, 1H), 6.85 (d, 1H), 4.29 (t, 2H), 3.54 (t, 2H), 2.34~2.25 (m, 5H)	
182	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [3-(4,5-dichloro-imidazol-1-yl)-propyl]-amide	3-(4,5-dichloro-imidazol-1-yl)-propylamine	3	δ 7.91~7.81 (m, 4H), 7.52 (s, 1H), 6.96 (d, 1H), 4.15 (t, 2H), 3.64 (t, 2H), 2.13 (q, 2H)	
183	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [3-(2-methyl-imidazol-1-yl)-propyl]-amide	3-(2-methyl-imidazol-1-yl)-propylamine	3	δ 8.11~8.09 (m, 3H), 7.61 (m, 2H), 7.45 (s, 1H), 6.88 (d, 1H), 4.31 (t, 2H), 3.46 (t, 2H), 2.25 (q, 2H), 2.33 (s, 3H)	
184	3	2-(2,4-dichloro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylicacid [3-(2-isopropyl-imidazol-1-yl)-propyl]-amide	3-(2-isopropyl-imidazol-1-yl)-propylamine	3	δ 8.10~8.05 (m, 3H), 7.58 (m, 2H), 7.40 (s, 1H), 6.88 (d, 1H), 4.22 (t, 2H), 3.60 (t, 2H), 3.02 (m, 1H), 1.3 (s, 6H)	

185	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (3-imidazol-1-yl-propyl)-amide	1-(3-aminopropyl)imidazole	3	δ 8. 89 (1H, s), 8.21 (2H, m), 7.83 (1H, d), 7.49 (1H, s), 7.38-7.24 (3H, m), 6.90 (1H, d), 4.31 (2H, t), 3.56 (2H, t), 2.38-2.33 (2H, m)	
186	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [3-(2-isopropyl-imidazol-1-yl)-propyl]-amide	3-(2-isopropyl-imidazol-1-yl)-propylamine	3	δ 8.26-8.21 (2H, m), 7.84 (1H, d), 7.65 (1H, s), 7.46-7.37 (3H, m), 6.88 (1H, d), 4.34 (2H, t), 3.62 (2H, t), 3.52-3.43 (1H, m), 2.27 (2H, m), 1.36 (6H, d)	
187	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [3-(4-methyl-imidazol-1-yl)-propyl]-amide	3-(4-methyl-imidazol-1-yl)-propylamine	3	δ 8.89 (1H, s), 8.21 (2H, m), 7.83 (1H, d), 7.43 (3H, m), 6.90 (1H, d), 4.31 (2H, t), 3.56 (2H, t), 2.38-2.27 (5H, m)	
188	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [3-(2-methyl-imidazol-1-yl)-propyl]-amide	3-(2-methyl-imidazol-1-yl)-propylamine	3	δ 8.29 (2H, m), 7.78 (1H, d), 7.49 (1H, s), 7.35-7.24 (3H, m), 6.70 (1H, d), 4.26 (2H, t), 3.64 (2H, t), 2.95(3H, s), 2.28 (2H, m)	
189	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [3-(2-ethyl-imidazol-1-yl)-propyl]-amide	3-(2-ethyl-imidazol-1-yl)-propylamine	3	δ 8.27 (2H, m), 7.79 (1H, d), 7.51 (1H, s), 7.33-7.25 (3H, m), 6.72 (1H, d), 4.27 (2H, t), 3.65 (2H, t), 2.90(2H, q), 2.28 (2H, m), 1.25 (3H, t)	

190	4	2-(4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [3-(4,5-dichloro-imidazol-1-yl)-propyl]-amide	3-(4,5-dichloro-imidazol-1-yl)-propylamine	3	δ 8.24-8.16 (2H, m), 8.04 (1H, d), 7.79 (1H, d), 7.45-7.33 (2H, m), 6.99-6.84 (1H, m), 4.18 (2H, t), 3.54 (2H, t), 2.18 (2H, m)	
191	5	2-(2,4-difluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [3-(2-isopropyl-imidazol-1-yl)-propyl]-amide	3-(2-isopropyl-imidazol-1-yl)-propylamine	3	δ 8.20 (1H, q), 8.18-7.97 (1H, m), 7.86 (1H, d), 7.64 (1H, s). 7.45 (1H, s), 7.39-7.24 (1H, m), 6.86 (1H, d), 4.33(2H, t), 3.60 (2H, t), 3.49 (1H, m), 2.26 (2H, t), 1.36 (3H, s), 1.34 (3H, s)	
192	5	2-(2,4-difluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (3-imidazol-1-yl-propyl)-amide	1-(3-aminopropyl)imidazole	3	δ 8.23 (1H, q), 7.13-7.97 (1H, m), 7.84 (1H, d), 7.74 (1H, s), 7.56 (1H, s), 7.31-7.24 (2H, m), 6.84 (1H, d), 4.40(2H, t), 3.56 (2H, t), 2.28 (2H, t)	
193	5	2-(2,4-difluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [3-(4-methyl-imidazol-1-yl)-propyl]-amide	3-(4-methyl-imidazol-1-yl)-propylamine	3	δ 8.22 (1H, q), 8.14-7.98 (1H, m), 7.84 (1H, d), 7.40-7.27 (3H, m), 6.85 (1H, d), 4.30 (2H, t), 3.57 (2H, t), 2.30 (5H, m)	

194	5	2-(2,4-difluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [3-(4,5-dichloro-imidazol-1-yl)-propyl]-amide	3-(4,5-dichloro-imidazol-1-yl)-propylamine	3	δ 8.19-8.03 (2H, m), 7.81 (2H, m), 7.39-7.29 (1H, m), 6.85 (1H, d), 4.17 (2H, t), 3.52 (2H, t), 2.16 (2H, t)	
195	5	2-(2,4-difluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [3-(2-methyl-imidazol-1-yl)-propyl]-amide	3-(2-methyl-imidazol-1-yl)-propylamine	3	δ 8.21 (1H, q), 8.06 (1H, m), 7.85(1H, d), 7.62 (1H,s). 7.39-7.27 (2H, m), 6.87 (1H, d), 4.30(2H, t), 3.58 (2H, t), 2.63 (3H, s), 2.25 (2H, t)	
196	5	2-(2,4-difluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [3-(2-ethyl-imidazol-1-yl)-propyl]-amide	3-(2-ethyl-imidazol-1-yl)-propylamine	3	δ 8.29-8.05 (2H, m), 7.86 (1H, d), 7.64 (1H,s). 7.43 (1H, s), 7.38-7.31 (1H, m), 6.95 (1H, d), 4.29 (2H, t), 3.57 (2H, t), 3.03 (2H, q), 2.25 (2H, t), 1.34 (3H, t)	
197	5	2-(2,4-difluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [3-(4,5-dichloro-imidazol-1-yl)-propyl]-amide	3-(4,5-dichloro-imidazol-1-yl)-propylamine	3	δ 8.19-8.03 (2H, m), 7.81 (2H, m), 7.39-7.29 (1H, m), 6.85 (1H, d), 4.17 (2H, t), 3.52 (2H, t), 2.16 (2H, t)	

198	6	2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (3-imidazol-1-yl-propyl)-amide	1-(3-aminopropyl) imidazole	3	δ 9.05 (1H, s), 8.00-7.88 (2H, m), 7.74 (1H, s), 7.66-7.57 (2H, m), 7.46-7.41 (1H, m), 6.95 (1H, d), 4.38(2H, t), 3.52 (2H, t), 2.25 (2H, t)	
199	6	2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [3-(4-methyl-imidazol-1-yl)-propyl]-amide	3-(4-methyl-imidazol-1-yl)-propylamine	3	δ 8.88 (1H, s), 8.00-7.87 (2H, m), 7.60 (1H, m), 7.41 (2H, m). 6.94 (1H, d), 4.28 (2H, t), 3.54 (2H, t), 2.29 (3H, s), 2.22 (2H, t)	
200	6	2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [3-(4,5-dichloro-imidazol-1-yl)-propyl]-amide	3-(4,5-dichloro-imidazol-1-yl)-propylamine	3	δ 7.94 (1H, m), 7.85 (1H, m), 7.76 (1H, s), 7.48 (1H, d). 7.30 (1H, t), 6.76 (1H, d), 4.17 (2H, t), 3.56 (2H, t), 2.16 (2H, t)	
201	6	2-(2-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [3-(2-methyl-imidazol-1-yl)-propyl]-amide	3-(2-methyl-imidazol-1-yl)-propylamine	3	δ 7.83 (1H, m), 7.50(1H, m), 7.39 (1H, s), 7.23 (2H, m), 7.13(1H, s), 6.76 (1H, d), 4.20(2H, t), 3.57 (2H, t), 2.47 (3H, s), 2.03 (2H, t)	

202	7	2-(3-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid [3-(4-methyl-imidazol-1-yl)-propyl]-amide	3-(4-methyl-imidazol-1-yl)-propylamine	3	δ 8.87 (1H, s), 8.37 (1H, d), 8.17 (1H, m), 7.83 (1H, d), 7.59 (1H, t), 7.40(1H, s), 6.84 (1H, d), 4.33 (2H, t), 3.60 (2H, t), 2.25 (5H, m)	
203	7	2-(3-chloro-4-fluoro-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (3-imidazol-1-yl-propyl)-amide	1-(3-aminopropyl) imidazole	3	δ 9.05 (1H, s), 8.37 (1H, d), 8.17 (1H, m), 7.83 (1H, m), 7.75 (1H, s), 7.61-7.43 (2H, m), 6.82 (1H, d), 4.41 (2H, t), 3.60 (2H, t), 2.30 (2H, t)	

Example 204: Preparation of 7-hydroxy-2-[4-(2-morpholin-4-yl-ethylamino)-phenyl]-1H-benzoimidazole-4-carboxylic acid [3-(4,5-dichloro-imidazol-1-yl)-propyl]-amide

(1) Preparation of 3-[(4-nitro-benzimidoyl)-amino]-4-methoxy-benzoic acid methyl ester

Anhydrous *p*-toluenesulfonic acid (6.30 g, 33.1 mmol) was added to 50 ml of benzene and the resulting mixture was refluxed while removing water using a dean-stock trap. Added thereto were 3-amino-4-methoxy benzoic acid methyl ester (3 g, 16.6 mmol) obtained in step 1 of Preparation Example 1 and 4-nitrobenzonitrile (2.94 g, 19.9 mol), followed by stirring at 160 ℃ for 8 hours. The resulting solution was cooled to room temperature, the reaction was stopped by adding $NaHCO_3$ thereto, extracted with ethyl acetate, the extract was dried over $MgSO_4$ and concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography to obtain the title compound (2.83 g, 8.59 mmol) in a yield of 52%.

^{1}H NMR ($CDCl_3$): δ 8.12-8.09 (m, 2H), 7.82 (d,1H), 7.70-7.69 (m, 1H), 6.98 (d, 1H), 4.91 (bs, 2H), 3.89(s, 6H)

(2) Preparation of 2-(4-nitro-phenyl)-7-methoxy-1H-benzoimidazole-4-carboxylic acid methyl ester

3-[(4-nitro-benzimidoyl)-amino]-4-methoxy-benzoic acid methyl ester (1.63 g, 4.95 mmol) was dissolved in 50% methanol, and 5% NaOCl was added dropwise thereto at room temperature. After checking the reaction by TLC, Na_2CO_3 (1.05 g, 9.38 mmol) was added dropwise thereto and refluxed for 40 min. The resulting solution was cooled to room temperature, extracted with ethyl acetate and the extract was concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography to obtain the title compound (0.75 g, 2.28 mmol) in a yield of 46 %.

^{1}H NMR ($CDCl_3$): δ 10.90 (bs, 1H), 8.36-8.31 (m, 4H), 7.95 (d, 1H), 6.78 (d, 1H), 4.16 (s, 3H), 4.01 (s, 3H)

(3) Preparation of 2-(4-amino-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid

2-(4-nitro-phenyl)-7-methoxy-1H-benzoimidazole-4-carboxylic acid methyl ester (0.63 g, 1.92 mmol) obtained in step 2 was dissolved in 15 ml of EtOH, 0.1 g of 10% Pd/C was added thereto and stirred for 24 hours while hydrogen was supplied thereto from a balloon fulfilled with H_2 gas. The resulting solution was filtered and dried to obtain the title compound (0.57 g, 1.92 mmol) in a yield of 100%.

^{1}H NMR (CH_3OH-d_4): δ 10.48 (bs, 1H), 7.93 (d, 2H), 7.82 (d, 1H), 6.77 (d, 2H), 6.71 (d, 1H), 4.11 (s,3H), 3.98 (s, 3H)

(4) Preparation of 2-[(2-morpholinoethyl)-4-amino-phenyl]-7-methoxy-1H-benzoimidazole-4-carboxylic acid methyl ester

2-(4-amino-phenyl)-7-hydroxy-1H-benzoimidazole-4-carboxylic acid (160 mg, 0.54 mmol) obtained in step 3 was dissolved in DMF, cesium carbonate (0.53 g, 1.61 mmol) was added thereto and stirred for 5 min. Added thereto were 2-chloroethylmorpholine (0.12g, 0.64mmol) and potassium iodide (0.18g, 1.08mmol), followed by stirring for 24 hours. Then, the resulting solution was extracted with ethyl acetate, the extract was concentrated under a reduced pressure, and the residue was purified by silica gel chromatography to obtain the title compound (91 mg, 0.22 mmol) in a yield of 41 %.

^{1}H NMR (CH_3OH-d_4): δ 7.97 (d, 1H), 7.57 (d, 2H), 6.77-6.73 (m, 3H), 4.54 (t, 2H), 4.11 (s, 3H), 3.99 (s, 3H), 3.57-3.55(m, 4H), 2.64 (t, 2H), 2.31-2.28 (m, 4H)

(5) Preparation of 2-[(2-morpholinoethyl)-4-amino-phenyl]-7-methoxy-1H-benzoimidazole-4-carboxylic acid-[3-(4,5-dichloro-imidazol-1-yl)-propyl]-amide

2-[(2-morpholinoethyl)-4-amino-phenyl]-7-methoxy-1H-benzoimidazole-4-carboxylic acid methyl ester (22 mg, 0.05 mmol) was dissolved in THF/H_2O, $LiOHH_2O$ (6.7mg, 0.16mmol) was added thereto and

stirred at room temperature. The resulting solution was filtered to remove residual $LiOHH_2O$, and the solvent was removed. The residue was dried and dissolved in DMF. Added thereto were 4,5-dichloro-1-(3-aminopropyl)imidazole (12.5mg, 0.06mmol), EDCI (30.9mg, 0.16mmol), DMAP (65.6mg, 0.54mmol) and HOBt (21.8mg, 0.16mmol), followed by stirring at room temperature. The resulting solution was extracted with ethyl acetate and concentrated under a reduced pressure. The resulting residue was purified by silica gel chromatography to obtain the title compound (19 mg, 0.03 mmol) in a yield of 63 %.

^{1}H NMR (CH_3OH-d_4): δ 7.93 (d, 1H), 7.77- 7.75 (m, 3H), 7.52 (d, 2H), 6.92 (d, 1H), 4.17 (t, 2H), 4.06-4.02 (m, 5H), 3.58-3.56 (m, 4H), 3.50 (t, 2H), 2.66 (t, 2H), 2.31-2.29 (m, 4H), 2.16 (q, 2H)

(6) Preparation of 2-[(2-morpholinoethyl)-4-amino-phenyl]-7-hydroxy-1H-benzoimidazole-4-carboxylic acid-[3-(4,5-dichloro-imidazol-1-yl)-propyl]-amide

2-[(2-morpholinoethyl)-4-amino-phenyl]-7-methoxy-1H-benzoimidazole-4-carboxylic acid-[3-(4,5-dichloro-imidazol-1-yl)-propyl]-amide (15 mg, 0.03 mmol) obtained in step 5 was dissolved in MC, BBr_3 (1.0M solution in MC, 0.3mL, 0.3mmol) was added thereto and stirred at room temperature for 48 hours. The reaction was stopped by adding water thereto and the resulting solution was extracted with MC/MeOH (7:1). The extract was concentrated under a reduced pressure and purified by silica gel chromatography to obtain the title compound (5.9 mg, 0.01 mmol) in a yield of 40 %.

^{1}H NMR (CH_3OH-d_4): δ 7.95 (d, 1H), 7.81- 7.79 (m, 4H), 7.55 (d, 1H), 6.94 (d, 1H), 4.15 (t, 2H), 3.94 (t, 2H), 3.59 (t, 2H), 3.58-3.56 (m, 4H), 2.64 (t, 2H), 2.32-2.30 (m, 4H), 2.18 (q, 2H)

Test Example 1: Assay for GSK-3β inhibiting activity

The GSK-3β inhibiting activity was determined in accordance with the method of Shultz et al. described in US Patent No. 6153618, with minor modifications by using phospho-CREB peptide as a substrate.

First, PCR (polymerase chain reaction) was carried out using human DNA as a template as well as primers which were designed to correspond to the 3'- and 5' ends of the polynucleotide coding human GSK-3β gene (Genbank Accession No.: L33801). The *Bam*H1/*Xho*I fragment of the amplified PCR product thus obtained was inserted into the pGex vector between the *Bam*H1 and *Xho*I sites, and the vector obtained was transformed into *E. coli* BL21(DE3). The transformed cells thus obtained was incubated in LB agar plates (1% Bacto-trypton, 0.5% yeast extract, 1% NaCl) containing ampicillin (100 ㎕/ml) until the optical density at 600nm reached about 0.5. The cultured mixture was cooled to 18 ℃ and isopropyl β-D-thiogalacto-pyranoside (IPTG) was added thereto to a final concentration of 0.5 mM. After 16 hours, the resultant was centrifuged at 10,000 x g for 10 min, the collected cells were suspended in a buffer solution (30 mM Tris-HCl (pH 7.5), 100 mM NaCl, 5% glycerol, 2mM DTT) and the cells were disrupted using Sonic Dismembrator (Fisher, U.S.A.) in a ice bath. The resulting solution was centrifuged at 16,000 rpm for 30 minutes. The supernatant was connected to GST (Glutathione-S-transferase) column (Pharmacia Biotech, U.S.A.) equilibrated in the same buffer solution, purified by glutathione affinity chromatography (eluent: 5 mM glutathione), and then, digested with thrombin to cleave the connecting site between the GST moiety and GSK-3β protein. The purified GSK-3β protein was diluted in a buffer solution (20 mM HEPES (pH 7.5), 5% glycerol, 2 mM DTT) to a final concentration of 50 mM NaCl and the resulting solution was subjected to mono S column chromatography (eluent: linear gradient from 0M to 1M NaCl buffer) using mono S column (Pharmacia Biotech, U.S.A.) equilibrated in the same buffer solution to obtain GSK-3β protein.

100 nM GSK-3β protein, 12.5 mM each of the compounds prepared in Examples 1 to 204 dissolved in DMSO, an assay buffer (50 mM Tris-HCl, pH 7.5, 10mM $MgCl_2$, 1mM EGTA, 1mM DTT), 100 μM phospho-CREB peptide (NEB, USA), 100 μM ATP, ^{32}P-ATP and 1 μ Ci were reacted at 30 ℃ for 1 hour. The reaction was stopped by adding 5㎕ of 5% phosphoric acid to 25 ㎕ of the resulting solution. The resulting mixture was centrifuged at 15,000 rpm for 10 min, 20 ㎕ of the supernatant was added dropwise to Whatman p81 filter paper, and then, the resulting filter paper was washed with 0.5% phosphate buffer for 10 min. The filter paper was further washed 3 times and the enzymatic activity was determined by examining the extent of phospho-CREB peptide phosphorylation which is

represented by the unit of count per minute (CPM), measured with a β-counter (Packard, USA).

The GSK-3β inhibiting activity was then calculated in accordance with the following equation:

$$\text{Degree of Inhibition (\%)} = 100 \times \left[1 - \frac{\text{CPM(sample)} - \text{CPM(blank)}}{\text{CPM(control)} - \text{CPM(blank)}} \right]$$

wherein the blank represents a value obtained without the use of the enzyme and the compound of the present invention, and the control, in the absence of the compound of the present invention.

The IC_{50} value of the inventive compound was determined from the degree of inhibition (%) and the result is shown in Table 3.

Table 3

Exam.	IC_{50} (μ M)	Exam.	IC_{50} (μ M)	Exam.	IC_{50} (μ M)	Exam.	IC_{50} (μ M)
1	>1	52	>1	103	>5	154	>1
2	>1	53	>1	104	>1	155	>1
3	>1	54	>1	105	0.05	156	0.28
4	>1	55	>1	106	0.015	157	0.49
5	0.3	56	0.7	107	0.05	158	0.23
6	>1	57	0.58	108	>1	159	0.68
7	>1	58	0.67	109	0.03	160	>1
8	>1	59	0.16	110	0.28	161	0.09
9	0.18	60	0.35	111	>1	162	0.24
10	0.04	61	>1	112	0.04	163	>1
11	>5	62	>1	113	0.19	164	0.84
12	0.2	63	0.45	114	0.001	165	0.08
13	0.36	64	0.03	115	0.026	166	>1

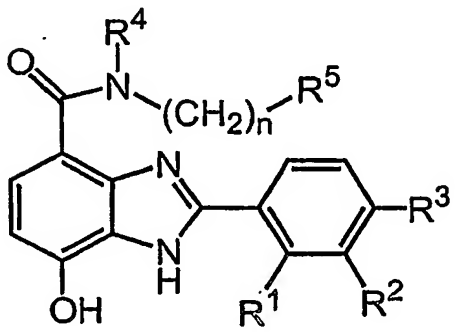
14	>1	65	0.06	116	0.003	167	0.1
15	0.11	66	>1	117	0.03	168	> 1
16	0.7	67	0.16	118	>5	169	>1
17	0.24	68	0.017	119	>5	170	0.19
18	>1	69	>1	120	0.07	171	>1
19	>1	70	>1	121	0.03	172	0.8
20	4.1	71	>1	122	0.2	173	0.1
21	>5	72	0.12	123	0.05	174	0.04
22	>1	73	>1	124	0.07	175	0.28
23	0.68	74	>1	125	>1	176	0.45
24	>5	75	0.009	126	>1	177	0.2
25	>1	76	0.05	127	0.18	178	0.04
26	>1	77	0.033	128	0.15	179	>1
27	>1	78	>1	129	0.12	180	0.21
28	0.74	79	0.12	130	0.33	181	0.03
29	0.08	80	0.07	131	0.17	182	0.008
30	>1	81	>1	132	0.19	183	0.06
31	>1	82	>1	133	>1	184	0.15
32	0.5	83	>1	134	0.04	185	>1
33	>1	84	>1	135	>1	186	0.05
34	>1	85	>5	136	0.24	187	0.01
35	0.007	86	0.25	137	0.005	188	0.002
36	>1	87	0.23	138	>1	189	> 1
37	>1	88	0.22	139	0.12	190	0.006
38	>1	89	0.32	140	> 1	191	0.09

39	>1	90	0.13	141	0.043	192	0.008
40	>1	91	>1	142	0.001	193	0.02
41	>1	92	0.08	143	0.002	194	0.004
42	>1	93	>1	144	0.006	195	0.03
43	>1	94	>5	145	0.002	196	0.02
44	>1	95	>1	146	0.07	197	0.003
45	0.02	96	0.022	147	0.21	198	0.02
46	>5	97	0.17	148	>1	199	0.01
47	>5	98	>1	149	0.14	200	0.002
48	>5	99	1	150	0.06	201	0.07
49	0.6	100	0.2	151	0.4	202	0.009
50	0.6	101	>1	152	0.24	203	0.003
51	0.87	102	0.23	153	0.05	204	>5

While the invention has been described with respect to the above specific embodiments, it should be recognized that various modifications and changes may be made to the invention by those skilled in the art which also fall within the scope of the invention as defined by the appended claims.

What is claimed is

1. A compound of formula (I), and a pharmaceutically acceptable salt, hydrate, solvate or isomer thereof:



I

wherein:

n is 0, 1, 2 or 3;

R^1, R^2 and R^3 are each independently hydrogen, hydroxy, halogen or morpholin-1-yl-ethylamino;

R^4 and R^5 are each independently hydrogen;

linear or cyclic C_1-C_6 alkyl optionally having one or more substituents, the carbon of the alkyl being optionally replaced with nitrogen, sulfur or oxygen, wherein the substituent is: hydroxy; halogen; alkyloxy; alkyl; amino; alkylamino; carboxyl; nitro; sulfonylamido; alkanesulfonyl; amido; an aromatic group optionally having one or more substituents selected from the group consisting of hydroxy, halogen, alkyloxy, alkyl, amino, alkylamino, carboxyl, nitro, amido, dioxoisoindole and sulfonylamino; an aromatic group having one or more substituents selected from the group consisting of hydroxy, halogen, alkyloxy, alkyl, amino, alkylamino, carboxyl, nitro and amido, the aromatic ring having nitrogen, sulfur or oxygen; or cyclic C_3-C_8 alkyl optionally having one or more substituents selected from the group consisting of hydroxy, halogen, alkyloxy, alkyl, amino, alkylamino, carboxyl, nitro and amido;

an aromatic group optionally having one or more substituents, the aromatic ring having optional nitrogen, sulfur or oxygen, wherein the substituent is; hydroxy; halogen; alkyloxy; alkyl; amino; alkylamino; carboxyl; nitro; sulfonylamido, alkanesulfonyl; amido; or linear or cyclic C_1-C_6 alkyl optionally having one or more substituents, the alkyl having an optional nitrogen, sulfur or oxygen linkage and the substiuent of the alkyl

being: hydroxy; halogen; alkyloxy; alkyl; amino; alkylamino; carboxyl; nitro; sulfonylamido, alkanesulfonyl; amido; an aromatic group optionally having one or more substituents selected from the group consisting of hydroxy; halogen; alkyloxy; alkyl; amino; alkylamino; carboxyl; nitro; amido; dioxoisoindole; and a sulfonylamino having an aromatic group substituted with hydroxy, halogen, alkyloxy, alkyl, amino, alkylamino, carboxyl, nitro, sulfonylamido, alkanesulfonyl or amido; an aromatic group optionally having one or more substituents selected form the group consisting of hydroxy, halogen, alkyloxy, alkyl, amino, alkylamino, carboxyl, nitro, sulfonylamide, alkanesulfonyl and amido, the aromatic ring containing nitrogen, sulfur or oxygen; or a cyclic C_3-C_8 alkyl optionally having one or more substituents selected from the group consisting of hydroxy, halogen, alkyloxy, alkyl, amino, alkylamino, carboxyl, nitro and amido; or

form, together with the -N-$(CH_2)_n$- moiety to which they are attached, a nitrogen heterocycle optionally having one or more substituents selected from the group consisting of OH, NH_2, NO_2, the heterocycle containing optional nitrogen or oxygen.

2. The compound of claim 1, wherein R^4 and R^5 are each independently hydrogen;

C_1-C_4 alkyl optionally having one or more substituents selected from the group consisting of OH, NH_2, NO_2, and an aromatic group, the aromatic group optionally having one or more substituents selected from the group consisting of OH, C_1-C_4 alkyloxy, NH_2, NO_2, methanesulfonylamino, ethanesulfonylamino, tolunensulfonylamino and dioxoisoindole; cyclic C_3-C_8 alkyl optionally having one or more substituents selected from the group consisting of OH, NH_2 and NO_2; C_1-C_4 alkyl carrying a morpholine or oxopyrolidine group which is optionally substituted with OH, NH_2, NO_2 or -O-; C_1-C_4 alkyl or C_1-C_4 aminoalkyl carrying a pyrrol, pyrazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, isoxazole, oxazole, isotiazole, tiazolidine, tiazole, 1,2,5-oxadiazole, 1,2,3-oxadiazole, 1,2,5-thiodiazole, 1,2,3-thiodiazole, 1,3,4-oxadiazole, 1,3,4-thiodiazole, pyridine, pyrimidine or triazine group which is optionally having one or more substituents selected from the group consisting of Cl, OH, NH_2, NO_2, C_1-C_4 and phenyl;

cyclic C_3-C_8 alkyl optionally having one or more substituents selected from the group consisting of OH, NH_2 and NO_2;

an aromatic group optionally having one or more substituents selected

from the group consisting of OH; NH_2; hydroxyalkyl; aminoalkyl; NO_2; and a C_1-C_4 alkyl group optionally having one or more substituents selected from the group consisting of OH, NH_2, NO_2, methanesulfonylamino, ethanesulfonylamino, tolunensulfonylamino, dioxoisoindole and thiophensulfonylamino; or

form, together with the -N-$(CH_2)_n$- moiety to which they are attached, a nitrogen heterocycle optionally having one or more substituents selected from the group consisting of OH, NH_2 and NO_2, the heterocycle containing 1 to 3 nitrogen, sulfur or oxygen atom.

3. The compound of claim 1, wherein R^4 and R^5 are each independently hydrogen;

C_1-C_4 alkyl optionally having one or more substituents selected from the group consisting of OH, NH_2, NO_2, morpholine, nitropyridineamino, pyridine, oxopyrolidin, imidazole optionally having a Cl, CH_3 or phenyl substituent; and phenyl optionally having one or more substituents selected from the group consisting of OH, NH_2, methoxy, NO_2, methanesulfonylamino, ethanesulfonylamino, tolunensulfonylamino and dioxoisoindole;

cyclic C_3-C_8 alkyl optionally having one or more substituents selected from the group consisting of OH, NH_2 and NO_2;

phenyl optionally having one or more substituents selected from the group consisting of OH; NH_2; NO_2; and C_1-C_4 alkyl optionally having a OH, NH_2, NO_2, methanesulfonylamino, ethanesulfonylamino, tolunensulfonylamino, dioxoisoindole or thiophensulfonylamino substituent; or

form, together with -N-$(CH_2)_n$- moiety to which they are attached, a piperidine ring optionally having one or more substituents selected from the group consisting of OH, NH_2 and NO_2.

4. A process for preparing the compound of formula (IA) which comprises the steps of:

reacting 3-amino-4-methoxy benzoic acid (compound II) and an alcohol to obtain compound (III);

adding anhydrous *p*-toluenesulfonic acid and benzonitrile to the compound (III) thus obtained, refluxing the mixture at 80 to 200 ℃, adding NaOCl thereto at room temperature and purifying by silica gel column

chromatography to obtain compound (IV);

dissolving the compound (IV) thus obtained in an alcohol, adding an aqueous alkali solution thereto and refluxing the mixture to obtain compound (V);

dissolving the compound (V) thus obtained in an organic solvent, adding a Lewis acid thereto and refluxing the mixture to obtain compound (VI);

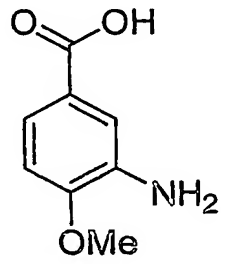
dissolving the compound (V) thus obtained in alcohol, adding a strong acid thereto at room temperature and refluxing the mixture to obtain compound (VII);

dissolving the compound (VII) thus obtained and (4-bromomethylphenoxy)-methyl polystyrene Wang resin in an organic solvent, adding a base and KI thereto and stirring the mixture at 50 to 60 ℃ for 1 to 24 hours to obtain compound (VIII);

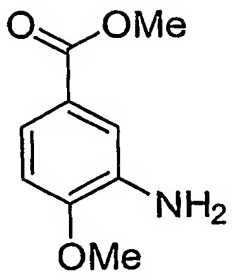
dissolving the compound (VIII) thus obtained in an organic solvent, adding an alcohol solution of an alkali hydroxide thereto and refluxing the mixture to obtain compound (IX);

dissolving the compound (IX) thus obtained in an organic solvent, adding $R^4N(CH_2)_nR^5$ and a coupling agent thereto and stirring the mixture at room temperature to obtain compound (X); and

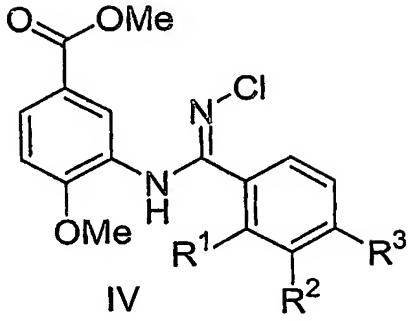
dissolving the compound (X) thus obtained in CH_2Cl_2, adding trifluoroacetic acid thereto and stirring the mixture at room temperature to obtain compound (Ia).



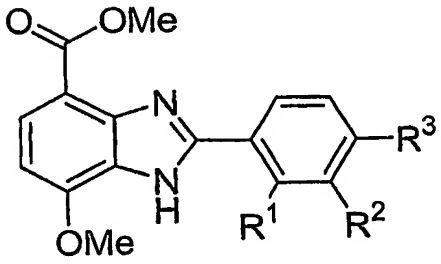
II



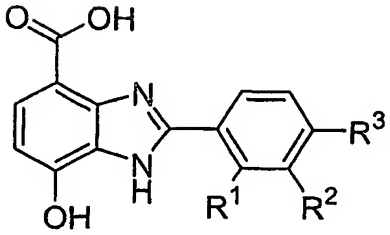
III



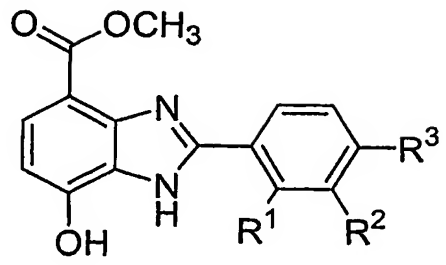
IV



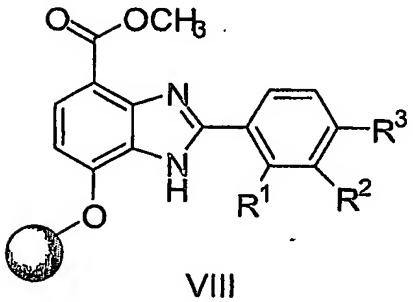
V



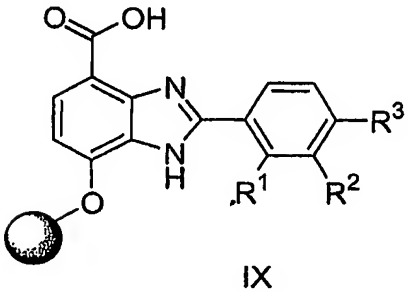
VI



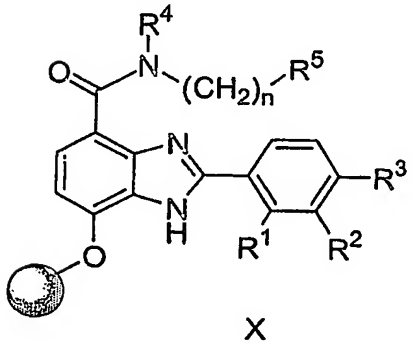
VII



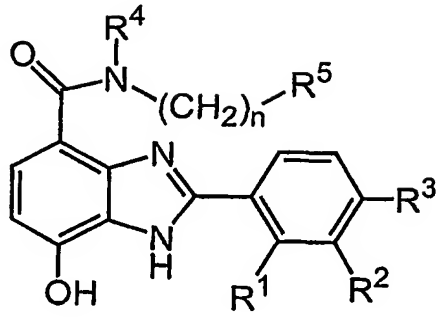
VIII



IX



X



Ia

wherein, n, R^1, R^2, R^3, R^4 and R^5 have the same meaning as defined in claim 1.

5. A process for preparing the compound of formula (Ib) which comprises the steps of:

reacting 3-amino-4-methoxy benzoic acid (compound II) and an alcohol to obtain compound (III);

adding *p*-toluenesulfonic acid, benzene and 4-nitrobezonitrile thereto, refluxing the mixture at 80 to 200 ℃, adding NaOCl thereto at room temperature and purifying by silica gel column chromatography to obtain compound (XI);

dissolving the compound (XI) thus obtained in an organic solvent, adding an aqueous alkali solution thereto, refluxing the mixture and purifying by silica gel column chromatography to obtain compound (XII);

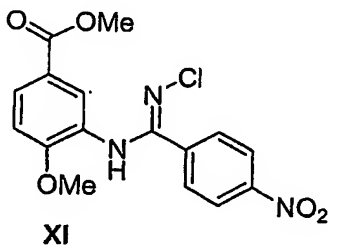
dissolving the compound (XII) thus obtained in an alcohol, adding Pd/C thereto and refluxing the mixture to obtain compound (XIII);

dissolving the compound (XIII) thus obtained in an organic solvent, adding a base, 2-chloroethylmorphine and potassium iodide thereto and stirring the mixture at room temperature to obtain compound (XIV);

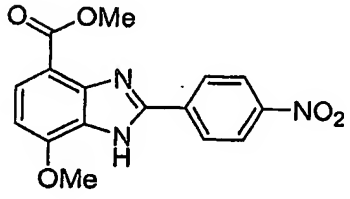
dissolving the compound (XIV) obtained thus in an organic solvent, adding an alkali hydrate, stirring the mixture at room temperature to obtain compound (XV);

dissolving the compound (XV) thus obtained in an organic solvent, adding 4,5-dichloro-1-(3-aminoprophyl)imidazole and a coupling agent, stirring the mixture at room temperature and purifying by silica gel column chromatography to obtain compound (XVI); and

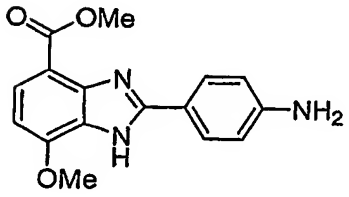
dissolving the compound (XVI) thus obtained in MC, adding a Lewis acid thereto, stirring the mixture, concentrating the resulting solution under a reduced pressure and purifying by silica gel column chromatography to obtain compound (Ib):



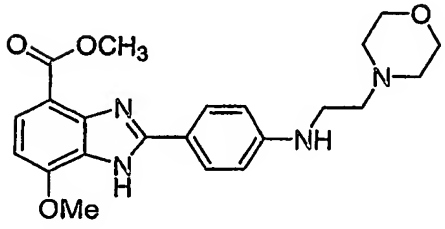
XI



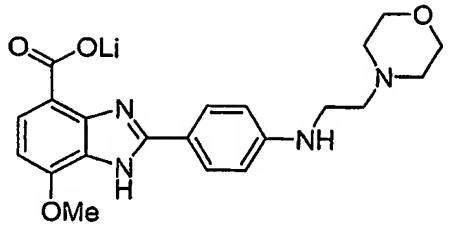
XII



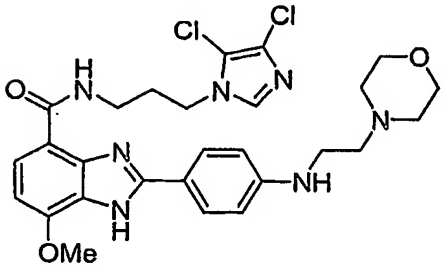
XIII



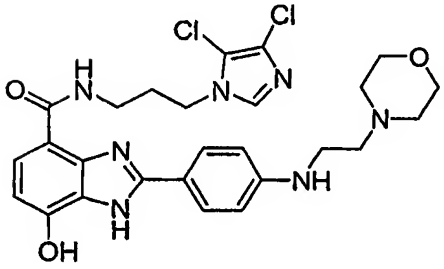
XIV



XV



XVI



wherein, n, R^1, R^2, R^3, R^4 and R^5 have the same meaning as defined in claim 1.

6. A pharmaceutical composition for inhibiting GSK-3β comprising a therapeutically effective amount of the compound of claim 1 and a pharmaceutically acceptable carrier.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/KR2004/000097

A. CLASSIFICATION OF SUBJECT MATTER

IPC7 C07D 235/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC7 C07D 235/18

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Korean patents and applications for inventions since 1975

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
CA-online, NCBI pubmed

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 95/07263 A (Schering Aktiengesellschaft) March 16. 1995 see entire document	1-3, 4-5, 6
A	US 5,821,258 A (Mitsui Chemicals Inc.) Oct. 13. 1998 see entire document	1-3, 4-5, 6
A	US 6,310,082 A1 (Newcastle University Ventures Limited) Oct. 30. 2001 see entire document	1-3, 4-5, 6
A	WO 2002/102978 A2 (Genentech Inc) Dec. 27, 2002 see entire document	1-3, 4-5, 6

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents,such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
28 JUNE 2004 (28.06.2004)	28 JUNE 2004 (28.06.2004)
Name and mailing address of the ISA/KR Korean Intellectual Property Office 920 Dunsan-dong, Seo-gu, Daejeon 302-701, Republic of Korea Facsimile No. 82-42-472-7140	Authorized officer LIM, Hea Joon Telephone No. 82-42-481-5590

Form PCT/ISA/210 (second sheet) (January 2004)